

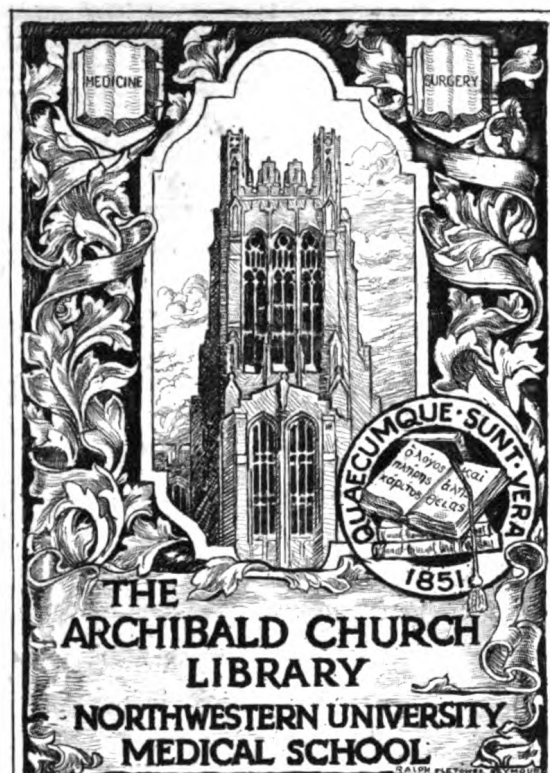
London County Council.

ARCHIVES OF NEUROLOGY
AND PSYCHIATRY

THE PATHOLOGICAL LABORATORY
LONDON COUNTY MENTAL HOSPITALS

MAUDSLEY HOSPITAL,
DENMARK HILL

VOL. VIII.



GIFT OF
Dr. J. G. Wilson.

Further Pathological Studies in Dementia Præcox.

ERRATA on page 14.

“aq. No 31 ” should read “ AgNO₃ ”

The Neurological Aspects of Shock.

ERRATA and ADDITION on page 4.

“ Colonel P. W. G. Sargent ” should read “ Major General Sir Cuthbert Wallace.”

ADDITION.

“ I have since found ruptured small vessels in the brain with microscopic hæmorrhages into the perivascular sheaths.”

F. W. M.



LONDON COUNTY COUNCIL.

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AND PSYCHIATRY

FROM THE

PATHOLOGICAL LABORATORY

OF THE

LONDON COUNTY MENTAL HOSPITALS,
MAUDSLEY HOSPITAL, DENMARK HILL.

EDITED BY

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Director of the Laboratory and Pathologist to the London County Mental Hospitals.

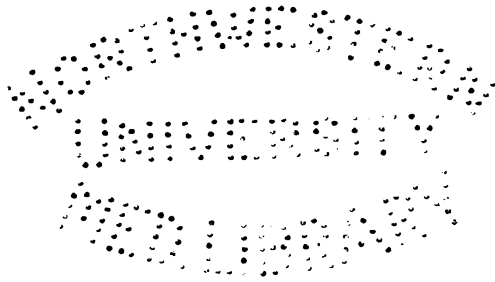
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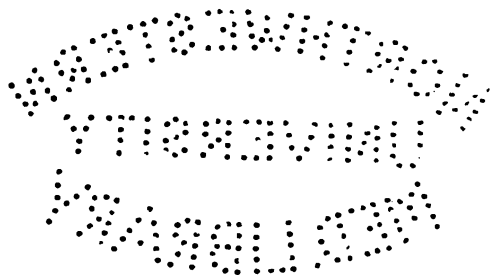
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PREFACE.

This volume contains an account of the work which has been carried on in the Laboratory of the Maudsley Hospital during the last three years, and consists for the most part of reprints of articles which have appeared in "The Proceedings of the Royal Society of Medicine," "The Journal of Mental Science," "The Lancet," "The British Medical Journal," and an excerpt from a special Report of the Medical Research Council. The only publications which have not appeared elsewhere are "Typhoid Carriers in Mental Hospitals" and the chemical abstracts.

The larger part of the volume is made up of studies in the pathology of Dementia Praecox; it would have been unwise to have delayed the publication of this work until the Archives were published, as much of it might have been anticipated; moreover, a limited circulation is not desirable for original investigations. Again, the cost of setting up type and providing illustrations is so enormously increased that the method adopted of republishing the researches carried out in the Pathological Laboratory in a book form is the most economic and practical mode of procedure.

By the aid of a grant from the Board of Control I have been enabled to produce the numerous costly illustrations to my articles on Dementia Praecox and republish the articles in this volume. Owing to the delay in opening the hospital for the reception of patients, I have been unable to further pursue the investigations on metabolism and oxidation processes in this disease. A study which, in view of the micro-chemical investigations I have carried out and preliminary unpublished investigations of the urine, is likely to be of fundamental importance, and for which I have received a grant of £400 from the Medical Research Council.

In conclusion I wish to thank all my collaborators, and Dr. Golla for allowing me to include his valuable Croonian Lectures embodying his researches carried out in this Laboratory and which he is still successfully pursuing.

My especial thanks are due to my assistant, Mr. Charles Geary, for the invaluable help I have received from him in the making of histological preparations and photomicrographs of the same; also to Mr. Sydney Mann for his valuable assistance in chemical problems, and help in the publication of this volume.

FREDERICK W. MOTT.

April, 1922.

MORISON LECTURES.¹

THE PSYCHOPATHOLOGY OF PUBERTY AND ADOLESCENCE.

BEING THE MORISON LECTURES, 1921, DELIVERED WITHIN
THE HALL OF THE ROYAL COLLEGE OF PHYSICIANS,
EDINBURGH,

BY SIR FREDERICK MOTT, K.B.E., M.D., F.R.S., LL.D. EDIN.

LECTURE I.—*March 7th, 1921.*

MR. PRESIDENT AND FELLOWS OF THE COLLEGE,—Permit me first to thank you for the great honour you have done me by inviting me again to deliver the Morison Lectures in this great seat of medical progress and learning.

The subject I have chosen is one that a previous lecturer illuminated ; needless to say, I refer to the late Sir Thomas Clouston, one of the great pioneers in psychiatry, who, by his clinical investigations, writings and teaching, did so much to spread light upon the causes, symptomatology and treatment of mental disease. In 1890 he delivered the Morison Lectures on "The Neuroses of Development." As he said, one of the objects of his lectures was "to show that the most serious of all the pathological facts of brain development are certain mental disturbances in the function of the brain, and that these are associated hereditarily and functionally with, and take their character from, the function of reproduction, which during adolescence is attaining its full strength." Our knowledge of the functions of the reproductive endocrine system was only in its infancy, but his practical mind regarding the relation of the physiology and pathology of reproduction to neuroses and psychoses is clearly shown throughout these lectures. Since then Edinburgh, by the investigations of its illustrious professor of physiology, Sir Edward Sharper Schafer and his pupils, have laid the foundation of endocrinology—a subject that has revolutionised our ideas of medicine, and

¹ Reprinted from the ' *Journal of Mental Science*, ' July, 1921.

which promises to illuminate the darkness of many diseases, including those of the mind. Again, I must not omit to mention the important pioneer clinical observations of Dr. Byrom Bramwell upon diseases having their origin in morbid conditions of the endocrine organs.

Every physician knows that there are two critical periods of life when insanity is especially likely to occur, *viz.*, the adolescent and the involutional—the periods when the sex instinct matures and wanes. Consequently there is *à priori* evidence suggestive of a correlation of the true psychoses with disorders of the sexual functions. The primal animal instincts of self-preservation, reproduction and the herd instinct are fundamental to all the mental and bodily activities of human beings. But Nature is unmindful of the individual, mindful only of the species, and Nature has ordained that the sexual impulse, during the reproductive period of life, should be the strongest of all physiological impulses, and the great source, but not the whole source, of psychic energy as Freud and his pupils maintained, for the war has conclusively shown that the instincts of self-preservation and the herd instinct are also great sources of psychic energy.

Feeling convinced that certain forms of mental disease were correlated with morbid changes in the reproductive organs, I determined to examine a series in the two sexes, but before any conclusions could be drawn, it was necessary to become familiar with the normal conditions of the human testis and ovary, at various ages from birth onwards, of individuals dying from various injuries or diseases, and then compare the same with those obtained from patients dying in the asylums.

The examination of the ovaries is much more difficult than the testes, for in order to see if there are ripening Graafian follicles they have to be cut in series. Dr. Laura Foster did this in 100 cases. Unfortunately she died abroad, and I published in vol. vii, *Archives of Neurology and Psychiatry*, her brief report with some additional remarks. I have since devoted a considerable time to a re-examination of her large collection of specimens. Also in conjunction with Dr. Hayao further specimens from fresh cases have been made and carefully examined. I will not take up your time with the details of methods, an account of which has already been published; I will only deal with such facts and principles as are involved in the discussion of the psychopathology of adolescence.

STRUCTURE IN RELATION TO FUNCTION OF THE REPRODUCTIVE ORGANS OF THE TWO SEXES.

Testes at birth.—The interstitial cells of Leydig are of mesodermic origin; they appear in foetal life, and exist before the sperm-cells have acquired their cytological characters. It is probable that they act as a ductless gland which plays a part in determining the male sex

characters in the indifferent germ plasm, in the normal development and maturing of the sex gland, in the formation of the accessory apparatus of the male genitals, and in the maintenance of those morphological and biological characters peculiar to the male sex. In support of these premises it may be mentioned that cryptorchids, in which the cells of Leydig are present but no spermatogenesis occurs, have sexual desire. Ligation of the vas deferens and X-ray treatment lead to destruction of the sperm-cells, but leave the interstitial cells and Sertoli cells uninjured, and the sexual desire persists. Cases of alveolar sarcoma of the interstitial substance have been recorded in which there was an extraordinary sexual precocity, which disappeared upon removal of the testes.

Structure of testis of newborn child.—Examination of the testis of a newborn infant shows the spermatic tubules, consisting of a delicate basement membrane containing closely-packed embryonic cells consisting of a nucleus with nuclear network surrounded by cytoplasm. The interstitial substance consists of loosely-packed connective tissue, blood-vessels and lymphatics, in which are groups of large polyzonal cells of Leydig, with a large round nucleus staining well with the basic dye. The surrounding cytoplasm stains pink with eosin and shows a number of minute vacuoles. These vacuoles contained lipoid granules, eosinophile, basophile and pigment (lutein) granules.

It is probable that during the period shortly following birth till puberty the interstitial cells of the infant are no longer active; their internal secretion has already performed its office of impressing upon the body the male characters and the special instincts and affective characters of the male sex. I will throw on the screen photo-micrographs of sections of the testes of males dying at various ages between birth and puberty.

The testis after birth till puberty.—At four months the interstitial cells are no longer seen. The seminiferous tubes have developed considerably by a proliferation of the embryonic cells, so that they appear nearly double the size of the tubes at birth. A few fine orange lipoid granules can be discovered in the seminiferous tubes and abundant scarlet-stained granules in the interstitial tissue. Only a few interstitial cells are now seen; they are smaller than in the testis of the infant at birth. The appearance of lipoid granules in the seminiferous tubes and in the interstitial tissue may be explained by supposing that it has been and is still utilised by the embryonic sperm-cells in their formative activity and proliferation; the interstitial cells will soon pass into the resting stage, in which they will remain till the beginning of puberty.

The testes of a boy, æt. 9, who died of shock from injury, exhibited similar microscopic appearances to the following, obtained from a boy, æt. 11, though less advanced.

The basement membrane of the tubules is more distinctly seen ; the tubes are larger than those of the infant of four months, they are close together, and there are observable evidences of formative activity ; the syncytial cells of Sertoli can here and there be differentiated, but they contain only few lipoid granules. The spermatogonia here and there have nuclei showing active mitosis. There is no interstitial lipoid observable, and the interstitial cells are still practically in the resting stage. It appears, therefore, that in the prepubertal stage of life the whole of the psychic and productive energy is absorbed in the normal individual, living under physiological conditions in building up a suitable body for preservation of the species by reproduction.

The ovary at birth.—In the female organ of reproduction we see a different order of things. A section of the ovary of a newborn child shows an immense number of primordial follicles lying in the exterior part of the stroma of the gland. It is calculated that there may be as many as 400,000. It may be presumed that each follicle with its contained ovum has a specific energy of its own ; now only a few relatively of these mature, and it may be assumed that those will mature which are endowed with the greatest specific energy, so that on this hypothesis there is a struggle for existence—a survival of the fittest—by which those with a weak vital energy are eliminated. For if one ovum escapes at each menstrual period it may be calculated that not more than 400 ova can fulfil their mission of escape from a ripe follicle, surrounded by syncytial nurse-cells derived from the discus proligerus. The female germ-cell is then taken to the uterus there to await passively the active male germ.

The Graafian follicle and maturation.—But whereas there is no prepubertal attempt at maturation of the male germ-cell, it is otherwise in the female, for sections of the ovary of a normal infant soon after birth may show complete Graafian follicles with liquor folliculi, zona granulosa and discus proligerus containing an ovum with zona pellucida. Surrounding the follicle may be seen the theca interna, and outside this the stroma with an increased vascularity.

We cannot in the human ovary discover cells corresponding to the interstitial cells of Leydig of the male and the cells of the theca interna and the epithelial cells within the follicle are considered by most authorities to be the source of an internal secretion in the human being.

Now these follicles which continue to mature during the whole prepubertal life of the normal healthy female do not proceed to dehiscence till menstruation occurs, but form atretic follicles, and these subsequently form small white corpora atretica. Why should these follicles undergo maturation, and what useful purpose could they serve seeing that the male reproductive organ remains at rest during the

prepubertal period? There is reason to think that both male and female characters are present in all the cells of the body, but the male characters are dominant. It is probable, therefore, that an internal secretion from the ripening follicles may impress and cause to persist the female characters of mind and body. Some recent experiments support this inference; for if the ovaries be removed from young hens they develop characters and behaviour which make it difficult to distinguish them from cockerels.

THE SEXUAL ORGANS AND VITAL ENERGY.

There is an intimate relation between the development of the sexual organs prior to puberty and the vital energy and resistance to disease. Kyrle's observations on a large number of cases show that a large number of children are born with undeveloped reproductive organs. Individuals with undeveloped reproductive organs have less vital resistance to disease than those with normal reproductive organs. Among the number dying with undeveloped seminiferous tubes far the greater number were physically undeveloped. The greater number of those dying in early life had undeveloped testes. I have found the same condition in the cases I have examined. But when I come to compare inborn germinal and acquired mental disease we shall see the same facts illustrated.

"It is characteristic of every living organism to build itself up according to a certain inherited type or pattern, so that we must attribute to its germ a formative capacity in virtue of which it turns to account both the food and the force which it derives from without." The capacity of the spermatogenic epithelial cells of the seminiferous tubules to form these dynamic vital units, the spermatozoa, in unlimited numbers for more than three-quarters the time of a man's life, illustrates remarkably well this power of the germ-cell to build itself up to a certain inherited type by a formative capacity, in virtue of which it is able to endow each spermatozoon with the formative capacity of building up the bodily and mental characters peculiar to species, race and individual ancestors.

SPERMATOGENESIS.

At puberty this active formative process of spermatogenesis commences, and examination of the testis shows the seminiferous tubes increased in size and closely packed together and the interstitial cells of Leydig are seen. Each tube shows a basement-membrane, within which and lying in it are the spermatogonia and the syncytial cells of Sertoli; these two cells have independent functions. From the former by active nuclear proliferation are formed the spermatocytes, from the

spermatocytes by hetero-typical nuclear division the spermatids—little masses of nuclear matter with half the number of chromosomes of the spermatocyte; there is thus preparation for conjugation with half the number of chromosomes (or nuclear matter) of the ovum. But this little particle of living matter endowed with such great potentialities is only in its infancy; it has, like the infant, to grow and acquire means of active locomotion, and the Sertoli syncytial cells filled with lipoid cholesterol ester granules nurse and feed the spermatids until they develop into free-swimming independent organisms.

Comparative examination of the seminal fluid in the vesiculæ seminales of a healthy boy, æt. 15, who died twenty-four hours after a motor accident, with the seminal fluid of a man, æt. 24, who died from injury the same day, showed that the spermatozoa were not so large and well developed in the former as in the latter. Moreover, examination of the testes of the two cases showed a greater abundance of lipoid granules in the syncytial cells in the adult of 24 than the boy of 15. It has been calculated that as many as 270,000,000 spermatozoa may be discharged at coitus, and it may be asked whence comes the material out of which all the highly phosphorised nuclear matter is formed. I have brought forward evidence to show that the lipoid granules seen in the interstitial tissue and in the cells of the tubules, especially the Sertoli cells, constitute the raw material from which the nucleic acid necessary for active nuclear proliferation and spermatogenesis is formed. These lipoid granules give the oxidase reaction owing to the presence on their surface of traces of unsaturated fatty acids. Decomposition and recombination processes are brought about by the catalytic action of the P and Fe of the cell nucleus upon the oxidase causing molecular oxygen, O_2 , to be converted into atomic oxygen, O-O, on the surface of the granules. I shall later on indicate the source of this phosphorised lipoid cholesterol ester. The experiments of Miescher and Kossel on the milt of Rhine salmon and other fish have shown that the heads of the spermatozoa consist of nucleic acid combined with a specific protamin. The tails consist of a lecithin cholesterol ester. Whence comes this phosphorised lipoid cholesterol ester?

THE BIO-CHEMICAL INTER-RELATION OF THE SEXUAL GLANDS AND THE DUCTLESS GLANDS.

We know that the interstitial gland can function independently of the genetic gland structure, and there is abundant proof to show that functionally correlated with the sexual glands are the thyroid, the parathyroid, the pituitary gland, the pineal gland, the adrenal, the islands of Langerhans of the pancreas; in fact, as Dr. Blair Bell, in his

very interesting work on the sex complex, maintains, the sex-glands enter into the hormonopoietic system, and, as Noel Paton asserts, act as a regulator and controller of that system. Abnormal conditions of the sex-glands may therefore disturb the whole hormonopoietic system, and dislocate the normal bio-chemical equilibrium necessary for their harmonious inter-relation that is essential for metabolism and the well-being of the body and mind.

THYROID AND REPRODUCTION.

There are many facts pointing to the bio-chemical inter-relation of the sexual glands and the ductless glands ; thus it is known that the thyroids increase in size during pregnancy ; there is indeed a distinct hypertrophy occasioned by a marked increase of colloid in the follicles. The development of the corpus luteum and the passage of its hormone into the blood may be the cause of this hypertrophy. An increase of the thyroid occurs at puberty, during menstruation and at the climacterium.

HYPOTHYROIDISM, PITUITARY HYPERTROPHY AND NEURONIC CHROMATOLYSIS.

I have examined the central nervous system in seven cases of hypothyroidism occurring in women at the climacteric period and found a marked decrease in the basophil chromatin substance of the central nervous system, the energy substance or kinetoplasm, and the association of the same in three cases with an acute manic-depressive psychosis. In two of these cases the ovaries showed an early active involution process with large numbers of recent atretic follicles. The pars intermedia of the pituitary was greatly increased, and throughout the pars nervosa were cells undergoing a colloidal transformation. What influence this increase of pituitary colloid may have on the central nervous system we do not know, but these cases show that an acute psychosis may occur in women, and that ovarian, thyroid and pituitary changes co-exist and may be causal in their symptomatic effects. Changes also occur in the parathyroids during pregnancy.

PITUITARY AND REPRODUCTION.

In the anterior portion of the pituitary, certain cells which normally exist in the gland are greatly increased in numbers and size and constitute the so-called pregnancy cells, which structural increase is partly the cause of the increase of weight of the gland in pregnancy. Dystrophia adiposo-genitalis or Frohlich's disease is associated with infantile genitalia and hypopituitarism.

CORTEX ADRENALIS AND THE REPRODUCTIVE FUNCTION.

There is evidence to show that one of the functions of the adrenal cortex, the cells of which are filled with a lipoid cholesterin ester, is to provide a substance for the building up of the myelin, but the following facts show that it has another very important function in connection with reproduction. The suprarenal body is developed early in embryonic life and is larger than the kidneys. The cortex adrenalis in the teleostean and elasmobranch fishes is a separate gland. The medullary portion with its chromaffin substance is a part of the sympathetic system, and may be regarded as a reserve store of energising adrenalin to be used when emergencies require it. The cortex adrenalis is developed close to, or forms part of the genital ridge, and in one of my cases of dementia præcox, where the testicle was absent on one side, the adrenal gland on that side was half the size of the other.

Cases of adenoma of the suprarenal cortex have been reported in which there was marked sexual precocity. In four male cases and two female cases of well-marked dementia præcox with regressive atrophy of the testis the adrenal cortex was narrower than normal and contained much less lipoid than normal.

Rats fed upon suprarenal gland showed hypertrophy of the testes; other organs did not show hypertrophy. Besides, therefore, serving as a store of phosphorised lipoid for laying down the myelin of the nervous system in the infant, it serves during the whole life of the individual as a store of lipoid supply to the reproductive organs, where it is taken by the blood to serve as the raw material necessary for formative nuclear activity.

Moreover it serves as the raw material from which the osmotic membranes of cells are formed, including the red blood-corpuscles, and it probably is a source of the antitoxins.

There is therefore abundant evidence to show the intimate interrelation of the reproductive organs, the thyroids, adrenals and the pituitary body. But the life of internal relation connected with the organic needs required for the preservation of the individual and the species, ultimately depends upon the sensori-motor activities of the life of external relation controlled by the brain, by which food and force are introduced into the body and transformed and utilised for the special purposes required.

THE INTERRELATION OF THE BRAIN AND REPRODUCTIVE ORGANS.

The harmonious interrelation of the brain and the reproductive endocrine system is effected by the autonomic vegetative nervous system, and this leads me to say a few words upon the interrelations of emotions and the reproductive functions.

The autonomic or vegetative system consists of three divisions: the cranial, sympathetic and sacral. When the neurones of the mid-division meet the neurones of either of the end divisions in any organ the influence of the two sets is antagonistic. Cannon has shown that all the bodily changes which occur in intense emotional states, such as fear and anger, occur as results of activity in the sympathetic division, and are in the highest degree serviceable in a struggle for existence likely to occur when these emotions are aroused. From this point of view emotional perturbations, which seize and dominate the organs and tissues, are expressive of an involuntary mobilisation of energy for making effective bodily reactions of the greatest importance for the preservation of life at times of critical emergency. During peaceful states of mind the cranial autonomic system controls the sympathetic by inhibitory influence. There is, therefore, a natural antagonism between the anabolic influence of the cranio-sacral (para-sympathetic) and the katabolic processes of the sympathetic—an antagonism correlated in the central innervations. Thus, when the mind or body is subjected to, or faced by noci-ceptor stimuli, giving rise to mental or physical pain, there is a diffuse automatic discharge of energy along the sympathetic division to effect self-preservation. Noci-ceptor stimuli and associations are stronger than bene-ceptor stimuli and associations in their influence upon the autonomic system; for emotional states caused by physical and mental pain antagonise and destroy pleasurable desires and their gratification, such as the relish and enjoyment of food and of sexual intercourse. Indeed, self preservation against injury or the preservation of the *amour propre* in a civilised community may be strong enough to dominate the field of consciousness. This was strikingly seen in the anxiety neuroses of officers during the war.

ANTAGONISM BETWEEN THE SYMPATHETIC AND THE SACRAL DIVISIONS OF THE AUTONOMIC SYSTEM.

Sexual excitement by thoughts or attractions of the opposite sex is consciously, but involuntarily, associated with an outflow of energy along the *nervi erigentes* of the sacral autonomic system; if there is an antagonism in the corresponding sympathetic division, such as occurs in fear or anxiety, erection cannot take place. Indeed, as Morton Prince has stated, the suppression of the sexual instinct by conflict is one of the most notorious experiences of this kind of everyday life. This instinct cannot be excited during an attack of fear or anger, and even during moments of its excitation, if there is an invasion of another strong emotion, the sexual instinct is at once suppressed. Under these conditions, as with other instincts, even habitual excitants can no longer initiate the instinctive process. The mental conflict which

occasions continuous contemplative fear and anxiety represses the sexual desire; this, however, is not a discovery by the new psychologists, nor is the influence of dreams in revealing a mental conflict; it is admirably told by Shakespeare in Lady Percy's speech to Hotspur.

But reproduction in the male is normally associated in nature with combat and pugnacity, and when tumescence occurs, excitement reaches its acme, and there is a diffuse discharge of energy along the sympathetic system, and a great liberation of muscular energy, rise of blood-pressure, accompanied by intense pleasure often mingled with a feeling of anger; the sympathetic discharge in the sacral region at the completion of the act of coitus overwhelms the sacral autonomic innervation, causing contraction of the seminal vesicles and the prostate with discharge of semen and detumescence.

THE SEXUAL INSTINCT AND REPRODUCTION IN RELATION TO PSYCHIC ENERGY AND INTEGRATION IN THE ADOLESCENT OF THE TWO SEXES.

Every fertilised ovum is potentially bisexual, possessing, however, a latent predominating tendency towards masculinity or femininity which decides the nature of the sex. There are many morphological evidences of this bisexuality in every individual; moreover, in some men there is a disposition towards femininity and in some women towards masculinity. The human body may be regarded as a very complex community of bisexual cells with differentiated structures and functions, which, originating from a single bisexual cell—the fertilised ovum—has during the phases of its development maintained its organic unity by a harmonious interrelation and integration of function effected by exciting and inhibiting subtle bio-chemical stimuli (hormones), conveyed by the circulating blood and lymph and by exciting and inhibiting bio-physical stimuli conveyed by the various systems of neurones constituting the cerebro-spinal and autonomic systems. The whole human organism, with its dominant male or female characters, constitutes the ego-complex or individual personality, which in its life of external relation is continually making conscious and unconscious adjustments to environment by its sensori-motor mechanisms, in subservience to the three primal instincts of self-preservation, of preservation of the species and of the instinct of the herd.

SECONDARY SEX CHARACTERS.

Up to puberty the mental and bodily activities are mainly directed towards the growth and development of the body, the capture of food, enjoyment of food and of play, and the avoidance of pain and injury; the psycho-physical energy is all absorbed in ministering to

the instinct of self-preservation, and the self-regarding sentiments are dominant. During this period the metabolism of girls is probably not very different from that of boys; the chemical processes are mainly engaged in growth of the body. With the onset of puberty and the maturation of the reproductive organs, the sexual hormones pass into the blood and impress on the body not only the visible sexual characters distinctive of male and female, but they reinforce in every cell of the body the predominant male or female characters, thus endowing the whole complex organism with an innately determined capacity not only to act and feel in a particular manner characteristic of the sex, but also to perceive the object upon which the action and feeling are directed in order to accomplish the supreme biological end—reproduction, and the preservation of the species. In adolescence the instinct of sex, male and female, pervades and appropriately energises all the organs and tissues of the body in the normal individual. But there are feminine men and masculine women in whom the instinctive energy of one sex does not wholly prevail, and males are met with having feminine tendencies in mind and body, and conversely females with male tendencies in mind and body. These tendencies are shown especially in the latest evolved human characters, and are therefore psychical, although frequently the secondary sexual characters are affected to some degree. A new and great source or spring of psycho-physical energy is brought into being at puberty and adolescence, and with it a complete mental revolution. The most obviously characteristic change is an increased interest in the opposite sex and in one's own sexual feelings and sex characters. The sexual instinct is, however, a foundation of altruism, for it embraces, even in animals, savages and primitive peoples something more than the self-regarding pleasure of gratification of the desire, which by moralists is called lust; for the sexual instinct would be biologically incomplete without the instinctive tender emotion of the male toward the female and offspring manifested by protection of them, and the still stronger instinct of protection and preservation of her offspring by the mother. The highest moral sentiments, indeed, have their roots in this primal instinct necessary for the preservation of the species.

When we realise that the intellect of man in the process of evolution has, within comparatively recent times, been superimposed upon this strong animal instinct, the gratification of which is attended with intense pleasure and its repression with a longing of unfulfilled desire and mental pain, and further when it is considered that social conditions and progress of modern culture and civilisation tend more and more to frustrate the end of this strong primal instinct, which Nature designed for the preservation of the species, a physiological disharmony arises which not only endangers the happiness and contentment of

mind of numbers of civilised human beings, but also threatens the race with decay. The herd instinct is intimately associated with the sex instinct in this problem, for the bond of union of the herd is a willingness on the part of each member to sacrifice individual interest and life in the interests of the herd. Self-preservation thus becomes secondary to preservation of the species.

THE CHANGE OF THE MENTAL ATTITUDE OF THE MALE AND FEMALE AT PUBERTY.

The change in the mental attitude of the male and female at puberty is shown by conduct in a variety of ways, but the emotions and passions are revealed in a similar manner by gesture language by all people, whether primitive or civilised; it is not surprising, therefore, that the psychoses and neuroses which affect human beings with an inborn neuropathic tendency dependent upon or correlated with disorders of repressed or perverted sex instinct present the same fundamental symptom-complexes in all human beings. But all psychic activities are subordinate to, and dependent upon, physiological processes, and I would put forward the premise that a disintegration of the psychic unity may be conditioned by a disintegration of the physiological unity. The functional correlation of mind and body is shown by the profound influence the reproductive endocrine system has in the evolution at puberty of the sentiments which have their roots in the sex instinct. Not only the highest altruistic sentiments of love, pity, and devotion, but the baser sentiments, *e.g.*, pride and vanity, arise from the biological instinct of self-display for attracting the opposite sex manifested by savages as well as civilised people by a regard for personal appearance and adornment by dress, ornaments and jewels.

Again, the cause of jealousy is usually resentment of the loss or suspected loss of the love of another for whom there is a sexual attraction which may find vent in hatred and vengeance. In the female these sentiments are more prolonged, more contemplative, and are felt more; and because she, unlike the male, is unable herself to react openly, impulsively, and violently upon her rival, the sentiment is generally repressed, causing a mental conflict which may end in a neurosis or psychosis. It is not surprising, therefore, that disappointed love is by no means an uncommon assigned cause of a mental breakdown. But sexual love cannot be separated from self-love, with which it constantly interacts, and a broken-off engagement, by wounding the *amour propre*, causes shame and humiliation, which the maiden represses and conceals because she expects little real sympathy from her own sex, and not infrequently she fears ridicule or contempt.

In adolescence the natural self-assertiveness of the young animal to

become independent and leave its parents to find a mate is shown in the human adolescent by vague longings and desires, while old affections are allowed to lapse; and this becomes a disturbing mental element, for it is not understood why the affections of parents and family and the home in which they were born and bred no longer satisfy the desires.

Attraction to the opposite sex when frustrated either by lack of opportunity or initiative often leads to a shut-in, brooding personality. The psychology of adolescence has been the inspiration to the poet, the novelist, and the dramatist. Adolescent love is the central subject of all romance. Shakespeare depicts the *joie de vivre*, the *élan vitale* in the young man of passion, Romeo, who by the attraction of Juliet says—“My bosom’s lord sets lightly on his throne, and all day long an unaccustomed spirit lifts me above the ground with cheerful thought,” and Hamlet, the melancholic introspective, highly intellectual young man of meditation and irresolution, who rejects Ophelia’s love with the words, “Get thee to a nunnery,” and Henry V, the young man of action, inspired by ambition, devotes all his psycho-physical energy to the conquest of France and the consolidation of his Kingdom by marriage with the French princess.

It would take too long to develop further this subject of the psychology of adolescence, but I will be content to quote two passages from Clouston: “We know as a fact that all the higher, emotional, intellectual, imaginative and volitional qualities of the brain arise between fourteen and twenty-five, and that the absolutely new and intense feelings connected with reproduction commence *de novo* during that time.”

After describing the visible morphological signs of a bad neurotic heredity Clouston states: “Doubtless by far the most important and subtle of the developmental defects are not those affecting the outward form of the body, nor the visible shape of the organs, but are those affecting the self-nourishing power and energising of the cells and the correlation of one centre to another.” It will be my endeavour in the following two lectures to support this hypothesis of Clouston by facts concerning the structural and functional changes in the reproductive system and the nervous system.

LECTURE II.—*March 9th, 1921.*

THE MORBID CHANGES IN THE REPRODUCTIVE ORGANS OF THE TWO SEXES COMPARED IN CERTAIN FORMS OF MENTAL DISEASE, GERMINAL AND ACQUIRED.

In my last lecture I dealt with the normal conditions of reproduction; in this lecture I propose to consider first “The Morbid

Changes in the Reproductive Organs of the Two Sexes compared in Certain Forms of Mental Disease, Germinal and Acquired."

By an investigation of the microscopic appearances of the testes in 100 cases of deaths occurring at all ages, from birth to eighty-six, in London asylums and various military hospitals, and of the seminal fluid in the vesiculæ seminales in a considerable number of these cases, the full account of which was published in the *British Medical Journal*, November 22nd, 29th, and December 6th, 1919, I was able to formulate certain general conclusions regarding spermatogenesis and its continuance in spite of advanced age and fatal microbial disease, even of prolonged duration, and I gave reasons for supposing that the lipid granules contained in the testes acted not only as the phosphorised raw material of nuclear activity and cell proliferation necessary for spermatogenesis, but as a protective barrier to the effects of circulating toxins.

EXAMINATION OF SEMINAL FLUID.

Examination by dark-ground illumination of the seminal fluid obtained from the vesiculæ seminales enabled one to observe some spermatozoa alive and active eight hours after death in two cases. One of these cases was a juvenile general paralytic, who died in an epileptiform seizure. Examination of dried films of the seminal fluid stained with hæmatoxylin eosin of a healthy man who died the same day from injury, showed the heads of all the spermatozoa stained by the basic dye, whereas in numbers of persons dying of various chronic diseases the majority of the spermatozoa were stained pink by the acid dye, indicative of a death change. May not this indicate a survival of the fittest spermatozoa in the vesiculæ seminales and a protective provision of Nature against fertilisation by weak organisms?

As a rule, in advanced cases of dementia præcox, the vesiculæ contained no spermatozoa. The spermatozoa showed in several of the early cases, in which the opportunity occurred for examination, marked degenerative changes (*vide* Plate I, fig. 1B).

EXAMINATION OF EMULSION OF TESTIS BY DARK-GROUND ILLUMINATION.

Now, examination by dark-ground illumination of the seminal fluid obtained from the vesiculæ seminales in thirty cases dying of tabo-paralysis and general paralysis has almost invariably shown some spermatozoa, generally in large numbers and even in cases of advanced ages—for example, one case of arrested general paralysis was æt. 69 at death. A variable number of the spermatozoa gave a normal staining reaction,

Emulsion of testis examined by dark-ground illumination showed that in the greater number of cases of general paralysis there was active spermatogenesis occurring in spite of advanced brain disease with its accompanying dementia and paresis.

EXAMINATION OF STAINED FILMS OF SEMINAL FLUID.

Films of the semen from the vesiculæ were stained and showed normally stained spermatozoa, together with large but varying proportions of degenerating forms. In no instance did the seminal fluid show the same deficiency in numbers of spermatozoa or such degenerated forms as in the semen contained in the vesiculæ seminales in the majority of cases of dementia præcox.

EXAMINATION OF SECTIONS OF TESTIS IN CASES OF GENERAL PARALYSIS.

Microscopic examination of sections of the testis of cases of general paralysis showed in a considerable proportion of the cases, in one and occasionally in both testes, strands and islands of completely atrophied tubules amidst normal tubules *with active spermatogenesis*. Seeing that where this atrophy occurred islands of normal Leydig cells could be found, it must be concluded that the atrophy of the spermatogenic tubules was not due to a general inflammatory syphilitic process, but probably to local inflammation and obstruction of the vasa efferentia by gonorrhœa or syphilitic infection or by arterial disease.

Now a comparison of the conditions found in this acquired disease—general paralysis—with conditions found in the vesiculæ and testes of cases of a germinal disease such as imbecility, idiocy and dementia præcox is striking.

EXAMINATION OF SECTIONS OF TESTES IN DEMENTIA PRÆCOX AND CONGENITAL IMBECILITY.

The testes of twenty-two cases of dementia præcox were examined, and for brevity I shall describe three stages of regressive atrophy, but they all merge into one another from the earliest stage, where there exists only slight morphological and bio-chemical changes in the heads of some of the spermatozoa (*vide* Plate I, fig. 2), and a diminution of the basophil staining of the nuclear substance of the spermatocytes, to a complete regressive atrophy of all the seminiferous tubes, leaving only the basilar membrane much thickened and a few syncytial cells of Sertoli, so that the microscopic appearances of sections of the organ as regards capacity for function in many of these advanced adolescent cases was less obvious than in the testes of an old man of eighty-six.

Indeed, the testis and seminal contents of the vesiculæ of an old man of eighty showed more evidence of virility than many of the earlier cases of dementia præcox. In more than half of the cases of dementia præcox there was a complete regressive atrophy and no evidence of spermatogenesis (*vide* Plates II-VII). As a rule it may be said that the earlier the onset of the mental symptoms the more likely was this complete regressive atrophy to occur; and it is quite possible some of these cases were prepubertal⁽¹⁾ in origin and spermatogenesis had never occurred, but this prepubertal condition certainly did not apply to a number of the cases of complete regressive atrophy. A long duration of the disease was the other factor which could be correlated with complete regressive atrophy. Speaking generally, the earlier the onset of mental symptoms and the longer the duration of life after their onset the more advanced was the regressive atrophy. In one case diagnosed adolescent mania and subsequently dementia præcox, I found numbers of spermatozoa in the vesiculæ; hardly any of them, however, presented a normal appearance and staining reaction. Sections of the testis showed active spermatogenesis, but when examined with an oil-immersion lens there were seen morphological and bio-chemical changes in the heads of many of the spermatids and immature spermatozoa.

Out of six cases I examined of congenital imbecility or idiocy, three of which were associated with epilepsy, 5 showed complete arrest of spermatogenesis. One case, a high-grade imbecile, showed active spermatogenesis, although death occurred from tuberculosis and broncho-pneumonia.

I do not deny that masturbation, which so many adolescent demented practise, may be a contributory factor in this regressive atrophy by the loss of seminal fluid and exhaustion of the phosphorised lipid, but I agree with Kraepelin that it is not the essential cause; for sexual excesses and excessive masturbation in other forms of insanity, e.g., general paralysis, do not cause this regressive atrophy. Moreover, we shall see that regressive atrophy of the ovaries occurs, and even if females suffering with this disease practised masturbation it would not cause exhaustion of the nervous system by loss of phosphorised lipoids.

The greater number of these cases of dementia præcox died of pulmonary tuberculosis, but we have seen that in other mental cases that died of pulmonary tuberculosis spermatogenesis was found; moreover, some of the cases died of acute lobar pneumonia after a few days' illness. Therefore tuberculosis cannot be assigned as the essential cause, although it may have been a contributory factor in the regressive atrophy of the reproductive organs in some cases.

⁽¹⁾ Kraepelin from clinical observations considers that there are prepubertal cases, and these are said to suffer from dementia precocissima.

EXAMINATION OF THE OVARIES IN MENTAL AND BODILY DISEASE.

Examination of the ovaries of 100 cases dying of various diseases do not give such clean-cut results as the testes, owing to the fact that chronic infective diseases have a more profound effect in preventing or arresting complete maturation of follicles, yet a comparative examination of the ovaries in cases of dementia præcox, congenital imbecility and epilepsy with other forms of mental disease, especially general paralysis, yielded similar results to those observed in the male sex; for the microscopic appearances of section of the ovaries are suggestive of a lack of specific vital energy of the reproductive organs in dementia præcox and congenital imbecility. But these diseases are due to an innate germinal deficiency, whereas general paralysis, an acquired disease, is due to an infection of the brain by the spirochæte of syphilis. Consequently, as might be expected, the ovaries of general paralytics who have died before the onset of involution do not exhibit a failure of the primordial follicles to undergo maturation, or, at any rate, not nearly to the same degree as in dementia præcox.

THE OVARIES IN DEMENTIA PRÆCOX AND GENERAL PARALYSIS.

To the naked eye the germinally deficient ovaries of patients suffering with dementia præcox and congenital imbecility are smaller and weigh much less than normal; sometimes they are no larger than those of an infant. Even in young females who have had a baby (and among my cases there have been none that have had more than one baby), the ovaries are much smaller than normal. The three or four cases that had had a pregnancy showed corpora lutea vera, but these were at least two years old, and there were no recent ones observable. The surface of the ovary of cases of dementia præcox had usually a white crinkled appearance, like a chestnut that had been peeled, and showed no superficial maturing follicular cysts. When the ovary is cut through the tissue is dense, and seldom shows any internal follicular cysts; sometimes the sections show a few old corpora lutea vera, but comparatively to the general paralytic or other forms of mental disease they are very few in numbers and small.

In many of the cases menstruation had ceased for some time, or there was a history of irregularity or amenorrhœa.

A similar state of regressive atrophy or failure of development was observed in a number of cases of congenital imbecility, especially when associated with epilepsy.

MICROSCOPIC EXAMINATION OF THE SECTIONS.

In dementia præcox there was no evidence of recent maturation of the primordial Graafian follicles, or if there were these follicles exhibited

appearances pointing to their soon becoming atretic. In some of the cases there was evidence of atretic follicles having been formed in earlier life by the existence of small corpora atretica such as may be found in the first year and later child life. The continuous zone of layers of primordial follicles found in early life, in some cases of congenital imbecility in the adolescent and in the normal adolescent female is not seen in dementia præcox. Instead one has to search for small groups of primordial follicles in the dense stroma. Sections stained for lipoid show that the ova are undergoing degeneration, droplets of fatty matter being seen in the cytoplasm and nucleus. Examination of sections stained to show the chromatin network of the nucleus and examined with an oil immersion lens showed appearances pointing to degeneration of the primordial follicles and replacement by the invading stroma. I will show a group of four, the best I could find, in a section where the greater number had disappeared. These show all stages of degeneration. One, the most healthy-looking, has had enough vital energy to have promoted the formation of a single enclosing layer of epithelial cells, but not enough to excite proliferation and produce a zona granulosa and discus proligerus, such as we find continually occurring in the ovaries of the infant. The other three ova show no commencing zona granulosa, and one is being invaded by the stroma (*vide* Plates VIII and IX). In general paralytic cases that died at an age under 37, including a case of juvenile general paralysis, we find a condition pointing to active reproductive processes analogous to those found in the male reproductive organ. For there are usually numbers of corpora lutea vera, showing that normal maturation and escape of the ovum had occurred, besides numbers of Graafian follicles going on to atresia, evidence of sufficient vital energy while the patient was suffering from the paralytic dementia to mature and form large and small atretic follicles—a condition which is not found, or only to a very limited extent, in dementia præcox.

WHY SHOULD THIS DEGENERATION OF THE GERM-CELLS COME ON IN ADOLESCENCE?

Dr. Laura Forster laid considerable stress upon the experiments of Ceni upon birds in support of the correlation of the dementia with changes found in the ovaries. He removed one hemisphere, and the birds surviving the traumatic shock were killed after varying periods of a few months to three years, and their ovaries were subsequently examined histologically. The primary shock had the effect of causing them to cease laying eggs for some months. In the following year they began to lay again, but in the second year fewer eggs were laid, or the birds ceased altogether from laying. The birds were otherwise in a

healthy condition. The examination of the ovaries showed a premature progressive involution. Ceni concludes that there are intimate relations between the brain and the ovary. It would have been interesting if Ceni had conducted similar experiments on male birds, and proved that lesions of the brain can produce a premature dynamic exhaustion of the testis. Inasmuch as in paralytic dementia one finds the reproductive organs exhibiting normal activity this conclusion of Dr. Forster does not hold.

The before-mentioned facts all show that in dementia præcox there is an inborn lack of specific energy in the germ-cells, and that relatively few have sufficient energy to mature; the great majority, therefore, die prematurely. The cases of dementia præcox that became pregnant and gave birth to a child and then developed the disease may be considered on the following broad biological grounds: The body is the vehicle for the germs, and whatever vital energy depending upon the sex instinct of reproduction remained in the mother was absorbed by the developing offspring. The regressive atrophy of the reproductive organs cannot be accounted as a direct cause of the mental and bodily signs and symptoms of this disease; otherwise castration would effect the same condition. It must, therefore, be only a part of a degenerative pathological process. If, however, we consider that the sex instinct necessary for preservation of the species pervades and energises in adolescence the whole of the bodily structures, and with the instinct of self-preservation constitutes the *élan vitale*, then we must regard the disease as a lack of vital energy of the whole body, but this lack is most manifest in the two functionally specialised organs most intimately connected with reproduction—*viz.*, the organ concerned in the production of the male or female germ-cells and the brain in their conjugation. In discussing the changes in the nervous system in my concluding lecture I shall deal with this part of my subject more fully.

If the subject be approached from an evolutionary point of view, we may consider that Nature, unmindful of the preservation of the individual and mindful only of the preservation of the species by survival of the fittest, would, by bringing on in adolescence a regressive atrophy of the reproductive organs, stop procreation of a degenerate stock.

NEUROPATHIC OR PSYCHOPATHIC HEREDITY.

Maudsley, in his *Pathology of Mind*, says:

"First that a person does not inherit insanity but a predisposition or tendency, and secondly, that the tendency comes from the stock. Nor need the unsound strain in the stock show itself in any form of actual insanity; it may appear in some allied nervous disorder, in

hypochondriasis and suicide, in feeble-mindedness, in dipsomania, in epilepsy in its manifold forms and other periodical nerve-storms, in eccentricity, in religious fanaticism, in the melancholic suspicious temperament, in selfish cunning, avarice and meanness."

Dr. Macpherson, in the paper to which I referred in my last lecture, says :

"The war has demonstrated what Maudsley long ago indicated—that one and the same cause may originate in neuropathic persons any of the various forms of psychoses or neuroses depending upon the particular temperament or idiosyncrasy of the individual. The acceptance of the view of the identity of the psychoses and neuroses would imply the belief that they share in common an inborn constitutional defect which is ineradicable and irremediable, of which the varying crises and the tendency to periodicity and recurrence are the phenomena."

It is not easy to decide whether a stock is neuropathic or psychopathic by ascertaining whether any member had been in an asylum, for any neurosis or uncertifiable psychosis or condition suggestive of mental instability would suffice to prove the existence of a germinal neuropathic tendency—the existence of which is not easily determined. The war has shown that a very considerable percentage of the male population are potential neuropaths, and it only required the necessary stress of fear and exhausting nervous strain to reveal the same.

NEUROPATHIC OR PSYCHOPATHIC INHERITANCE IN RELATION TO THE INSANITY OF ADOLESCENCE.

It is generally admitted that adolescent insanity is much more likely to occur in stocks where there is a recognisable or known neuropathic or psychopathic hereditary predisposition. But cases of dementia præcox occur in stocks where there is no ascertainable hereditary taint. It occurs also in primitive races. How can we account for this it might be asked? When we consider that at each coitus there may be over 200,000,000 spermatozoa ejected, each with its own specific energy, chance comes into play as regards fertilisation of the ovum by a spermatozoon carrying characters varying from the normal in the latest and highest products of evolution. Again, it may be that one of three or four hundred ova that can escape into the uterus to be fertilized may carry a variation from the normal and become fertilised ; or, again, it may happen that a variation arises from incompatibility of the determinants conveyed by the male and female germs. Such a hypothesis would explain why a genius or an imbecile may arise from the union of two reputedly sound stocks.

But there is always the question whether these evolutionally latest developed characters or the vital energy of the whole body may not be

modified adversely in the germ-cells of a healthy stock by the prolonged toxic influence of such race poisons as alcohol, syphilis and tubercle, and whether this variation can be transmitted as an acquired character. I have already given reasons why this assumption is doubtful from the examination of the seminal fluid and testes in a large number of cases of syphilis and chronic infective diseases such as tuberculosis, chronic dysentery, etc. Some authorities have asserted that syphilis may in this way cause dementia præcox. As far as my observations go I have not found cases of dementia præcox give a plus Wassermann reaction, either of the blood or fluid. Moreover, syphilis is a very common disease. Undoubtedly congenital syphilis causes imbecility and juvenile general paralysis, but this is due to the presence of the spirochætes in the brain. In a number of cases of juvenile general paralysis normal spermatogenesis and follicle formation may be found. Moreover, dementia præcox occurs in races where syphilis is unknown.

Dr. John Macpherson has recently in an interesting article on the "Identity of the Psychoses and Neuroses" shown that primitive people in all parts of the world suffer with nervous affections of germinal origin, but they do not suffer with such acquired diseases *e.g.*, general paralysis, unless they be syphilised. Naturally racial and environmental conditions give a particular or local colour to the neuroses and psychoses, but fundamentally they have the same symptomatology. Both Kraepelin and Van Brero point to the fact that dementia præcox is a common affection among the native Javanese, and the former ascertained that auditory hallucinations are not commonly met with. Probably this can be accounted for by the fact that these people being analphabets, their mental furniture consists largely of concrete images, rather than abstract linguistic symbols. The expression of thoughts and feelings by language of graphic and auditory symbols is a recent development comparatively to the language of the emotions. For the same reason probably dreams are usually visual representations rather than auditory.

Maudsley has remarked that Nature tends to end or mend a degenerate stock. How could this be brought about?

(1) By rendering the psycho-physically weak infertile. This I have shown actually occurs in the case of a large proportion of cases of dementia præcox and congenital imbecility, especially when the latter is combined with epilepsy.

(2) By segregating in relatively a few of the germ-cells the unsound elements, by a coalescence of similar diseased germinal determinants, as it were by a crystallisation. This would not only purify the stock by segregation of the diseased elements, but by concentration in a few of the offspring it would lead to intensification and antedating of the onset of the disease.

We have seen that Kyrle's results indicate that young male children with an insufficient vital energy of the germ-cells to carry them beyond the infantile stage perish from disease. In the female reproductive organ the ova that undergo complete maturation and escape are relatively few; all the rest perish. This may mean a concentration of all the vital energy in the ova with the greatest potentialities.

THE CONDITION OF THE ENDOCRINE GLANDS IN DEMENTIA PRÆCOX.

The pituitary body has been examined in the few cases in which this organ was sent to me. Generally speaking the organ seemed small, not weighing more than 0.5 grm. So far I have been unable to discover any constant morbid change, but I have only examined the gland in a few cases.

The thyroid.—As a rule the weight of this gland was below normal, but here again I am not prepared to associate the change in the reproductive organs with any constant microscopic changes in this gland.

The adrenal glands.—The adrenal glands compared with cases of general paralysis and other forms of insanity dying in adolescence exhibit indications of a cortical deficiency in dementia præcox recognisable to the naked eye; for the gland is diminished in weight and thickness, and when cut through the cortex is considerably thinner than in the normal. The glands from six cases have been examined microscopically by staining sections, cut with the freezing microtome; these undoubtedly showed a diminution of the lipoid cholesterol esters in the cortical cells, especially of the zona fasciculata, but inasmuch as the lipoid of the cortex subserves many other functions than that of supplying lipoid cholesterol esters for the function of reproduction, notably as Elliot has shown in the production of antitoxins, it follows that even here there is no definite proof that this deficiency can be associated with the failure of the reproductive function. I fully realise the inadequacy of this part of the research carried out upon the endocrine system, but it seems to me to be of such fundamental importance that I hope to attack the problem by inducing medical officers to study their cases carefully during life by modern clinical methods associated with experiments on the respiratory exchange and metabolism in conjunction with my assistant, Capt. Sydney Mann, B.Sc., in the Pathological Laboratory of the Maudsley Hospital. This work should have commenced ere this but for the delay in utilising the hospital for the purpose its founder, Dr. Maudsley, intended.

OXIDATION PROCESSES IN THE BRAIN AND REPRODUCTIVE ORGANS.

There are many morbid anatomical and microchemical conditions found in the reproductive organs and the brain strongly suggestive of

deficient oxidation processes, which, combined with low blood-pressure, would cause a deficiency of psycho-physical energy in all the organs and tissues of the body, but especially would deficiency of oxidation processes affect the functioning of the reproductive organs and the brain with its different functional levels. There is some evidence in favour of this view, for Koch and Mann, working in the Claybury Laboratory, examined, at my suggestion, chemically the brains of nine cases, seven of which were cases of dementia præcox, and found a diminution of neutral sulphur independent of the cause of death and not found in other forms of insanity. These authors say: "It would not seem improbable to suppose that the subject of this mental disorder may possess a general bodily inherent deficiency for oxidation processes. Examination of other tissues of the body for neutral sulphur and its proportion to the total sulphur contents would help materially to decide this point. In the meanwhile some support to this view of a general inherent bodily deficiency for oxidation processes is afforded by Pighini's observations on the increase of neutral sulphur in the urine in this disease. It is obvious that an investigation of the hormono-poietic system needs an intensive study of a few cases by clinical chemical methods during life, followed by a thorough histological and chemical investigation of the ductless glands after death, the results to be compared with the results obtained by an investigation upon mentally normal persons suffering with similar fatal bodily diseases.

ANTEDATING OR ANTICIPATION.

From the study of numerous pedigrees I came to the conclusion that there was a tendency for insanity not to proceed beyond three generations. There is frequently either an apparent regression to the normal type or the stock dies out. Not infrequently the stock dies out by the inborn tendency to insanity manifesting itself in the form of congenital imbecility or in the insanity of adolescence. Such patients are, as I have shown, usually infantile, and are prone to die of tuberculosis; or if they are capable of procreating, their anti-social behaviour brings them into the asylum. Among primitive people the struggle for existence would be more severe than among civilised people and such cases would perish in various ways.

Morel, in 1859, pointed out that progressive uninterrupted transmission leads finally to special degenerative forms, to imbecility and idiocy, and with the diminished capability of propagation of the latter kind the stock therefore gradually becomes extinct. Antedating and intensification of heritable disease or predisposition to disease would not only lead to diminished vital resistance to poisons or germs of disease, such as alcohol, syphilis and tuberculosis, but also, owing to

lack of physical and mental ability to obtain the necessities of life, vital resistance is still further diminished ; so that the tendency is for the unsound members of the third or fourth generation of a mentally degenerate stock to die at a comparatively early age of some inter-current disease, especially tuberculosis, and thus propagation is prevented.

Unfortunately during the Great War these neuro-potentially unsound persons, of the great numbers of whom the pensions bill the Nation is paying is the best proof, were not fit for the front line, and were not therefore killed off to anything like the degree that the A1 physically and mentally sound men were.

The war in this respect, therefore, has not had the purifying effect that it had in ancient times when in the struggle for existence the mentally and physically strong alone could survive. In this country of doles to the unemployed, of whom a large percentage through mental or physical deficiency are unemployable, there is every opportunity given to the prolifically fertile high-grade moral and intellectual imbecile to propagate.

STATISTICS OF ANTEDATING.

In 1911 I published statistical data relating to the ages of onset of insane offspring and of insane parents. This was based upon a card system relating to 3,118 relatives who had been admitted into the London County asylums and made up from 1,450 families.

This analysis showed a signal tendency to the occurrence of insanity at a much earlier age in the offspring than in the parents. The accompanying graph is based upon 508 pairs of parents and offspring ; there were 464 insane parents and 508 offspring. Some of the parents had more than one insane offspring. All forms of insanity occurring in the offspring were included, as were all forms in the parents. In 1917, the analysis of the relative cards since 1911—a period of six years—was limited to insane parents and offspring in which a diagnosis of dementia præcox was made.

The numbers of cases were considerably diminished, as might have been expected, for in some of the London asylums the term "dementia præcox" was not employed, and only in comparatively recent times has it come into existence. The graph which I show is similar in its characteristics as regards the curves of the age of onset of the parents, but in respect to the age of onset of the offspring, instead of 47·9 being under 25 upon admission, 75 per cent. of the cases suffering with dementia præcox were admitted under the age of 25.

Seeing that a great many cases were either insane before certification or by their conduct had given prodromal evidence of oncoming insanity, it is probable that practically all the cases commenced before the

termination of the adolescent period of life. It will be noted that the parent's graph resembles very much that of a graph of the total admissions to the asylums.

The number of female offspring of insane parents suffering from dementia præcox are more numerous than the male offspring of insane parents, and the antedating is more pronounced, *viz.*, 23·67 years in the females to 17·81 in the males. Now that the war is over and medical officers better trained in psychological medicine in the asylums, it is hoped that more reliable records of diagnosis will be possible. Still, certain facts seem to come out, *viz.*, that dementia præcox is a disease of adolescence and that females are affected more than males; moreover many cases that commence in adolescence do not die for many years, in fact, some authorities would regard this as one explanation of the greater number of chronic cases on the female side in asylums, another factor being that general paralysis which is fatal in a few years is about four or five times as common among males.

Now why should dementia præcox affect females more than males as these statistics seem to indicate?

Firstly, the physical exhaustion of pregnancy: in quite a considerable percentage of cases of which I have examined the ovaries, mental symptoms came on after the birth of the first and only child. Secondly, the enforced frustration in a much larger number of women than men of the sex instinct and its biological end by modern social conditions. Another explanation may be offered why there have been more female cases of dementia præcox during this period admitted to the asylums than males is this: The whole male population was conscripted and a number of potential cases of dementia præcox were recruited; some were killed, some died of disease, others found their way into the military hospitals for nervous and mental diseases.

Inasmuch as this disparity of affection of the two sexes is not in accordance with pre-war experience this explanation seems much the more probable.

LECTURE III.—*March 11th, 1921.*

In my last lecture I dealt with the regressive atrophy of the reproductive organs; in this lecture I intend to describe the changes in the central nervous system, and endeavour to show how these two morbid changes may throw some light on one of the most important diseases of the mind.

The critical periods of life I have shown as regards mental disease are adolescence and the climacteric periods of life when the sexual function matures and wanes, and this alone affords *à priori* evidence of the important relations between the sexual functions and mental disease.

The question naturally arises whether the regressive atrophy of the sexual organs is the cause of the mental symptoms or is correlated with them.

(a) By a disturbance of the normal physiological equilibrium of the reproductive and endocrine glands, with a resulting toxæmia.

(b) By the suppression of the normal sexual libido and the psycho-physical energy associated with the sex instinct.

(c) By a germinal bio-chemical failure of the nuclear matter of the cells of the body generally, but of the reproductive organs and the brain in particular, associated with deficiency of oxidation processes and a corresponding deficiency of reproductive and psycho-physical energy.

I shall endeavour to show that the last premise is the essential cause, but that the first two are consequent and co-operate.

The arguments I would adduce are as follows :

(1) There is a general lowered vital reaction of the tissues to disease, anergic symptoms and low blood-pressure, and early cessation of reproductive powers. The amount of neutral sulphur in the brain is diminished, indicative of diminished oxidation processes.

(2) The morbid changes in the nervous system are most marked, and especially affect the nuclei, cytoplasm and dendritic processes of the neurones of both the first and second type of Golgi. The fibres are scarcely affected at all, indicating that the neurones are for the most part not dead, but fail to function. These changes and their significance when compared with the changes met with in an acquired disease, *e.g.*, general paralysis, may best be explained by a failure of function due to an insufficiency of oxidation processes involving the molecular oxygen brought by the blood-streams being converted into free atomic oxygen—by the katalytic action of the nucleus upon the oxidase granules.

(3) A number of cases of dementia præcox show prepubertal clinical signs with history of arrest of development of mind which can be explained by arrest of development of cortical neurones, and at puberty when the stress of productive energy of the reproductive organs occurs nuclear neuronic failure again shows itself by the onset of fresh symptoms of mental defect and disintegration of the psychic unity. This nuclear decay or loss of durability is of germinal origin, for there is simultaneously a progressive failure of nuclear formative activity in the organs of reproduction. At what period in early life this nuclear failure of the brain and reproductive organs occurs it is difficult to determine in individual cases, but I am of the opinion from histological observations that it begins in some cases before puberty—even long before puberty—and Kraepelin points to the fact that in many cases clinical symptoms occur in prepubertal life, so that it is legitimate to conclude that there are a number of cases which might be termed “dementia præcossissima.”

Before proceeding further it is necessary to call your attention to certain anatomical and physiological premises upon which I shall base my arguments regarding the psycho-pathology of dementia præcox.

THE OXIDASE REACTION.

If a portion of the brain or a section of spinal cord taken from an animal immediately after death be stained for the oxidase reaction the grey matter is coloured blue, the white matter is unstained.

Marinesco has demonstrated that histological examination of the sections shows that the cytoplasm of the ganglion cells, as well as their protoplasmic prolongations, are studded all over with fine blue-stained granules. Neither the nucleus nor the axis-cylinder process contains any trace of granules. This agrees with the observations made by this author and myself in respect to the absence of refractile granules in the nucleus and axon when a living nerve-cell is examined with the ultra-microscope. Marinesco found these granules in the cells of the choroid plexus, but none in the neuroglia cells. Marinesco remarks it is probable that these oxidase granules belong to the neurone terminals which constitute the synapse and establish connections between the different neurones.

"It is especially in the plexiform layers, as is the case for the so-called granular layer of the cerebellum and of the brain, that these oxidase granules are very numerous."

These facts clearly indicate that oxidation processes take place in the grey matter, and that the intercalary cells, Type II Golgi (granules), which form the physiological link in systems of neurones of the first type, play an important part in the chemico-physical processes of the synapses.

Now if oxidation processes which occur in the grey matter are essential for all nervous activity (including psychical), and if it be that molecular oxygen of the oxidase granules must be converted into free atomic oxygen to ensure neuronic function, it follows that deprivation of oxygen carried in the circulating blood will cause suspension of function. This is the case, for Mosso has shown, in a patient of his who had been trephined, that unconsciousness invariably occurred six seconds after pulsation in the brain had been caused to cease by compression of both carotid arteries.

It is calculated that there is six times as much blood in the grey matter as in the white matter. It was asserted by Leonard Hill that the oxygen content of the blood leaving the brain was as great as that of the blood entering. Bayliss gives reasons why this conclusion is not valid. Moreover, it must be remembered that the amount of grey matter to white matter in the brain is relatively small, and we know that no active oxidation processes take place in the white matter. This

fact also disposes of the argument that Battelli's observations show that relatively to other organs in the body the peroxidase reaction of the brain is feeble.

It may be concluded, therefore, that oxidation processes are essential for neural function, and that oxygen for cerebral activity is continually being used up and replenished by the blood. I have shown that there is no free oxygen in the cerebro-spinal fluid, but there is as much CO_2 free and combined as in the lymph. If the neurones are bathed by the cerebro-spinal fluid, the sugar in the fluid may be a source of energy for the nervous system and be continuously undergoing a process of oxidation.

Now to continue the argument, we may assume the following premises :

All psychical processes are subordinate to physiological processes—that is neural activity.

All neural activity is dependent upon oxidation processes. These oxidation processes occur in the grey matter.

Oxidation processes are dependent upon the liberation of atomic oxygen from oxidase granules.

The oxidase granules are found on the body of the cell and the dendritic processes. They are especially abundant in the granule layers of the brain and the cerebellum. These granules are the intercalary neurones, second type of Golgi, and where they form definite layers they are interposed between radial fibres and the dendrites of neurones of the first type of Golgi forming a synapsis.

Granted Marinesco's observation, that in the granular layer the oxidase granules are especially abundant, it will be here especially that the atomic oxygen will be abundantly liberated under the influence of a nuclear catalase ; for these cells consist mainly of nucleus.

If the iron or phosphorus of the nucleus or both act as a catalyser, as there is reason to believe, it may be hypothesized that when a stimulus arrives at the layer of intercalary neurones a catalase is liberated from the abundant nuclear substance ; this acts upon the molecular oxygen attached to the oxidase granules, converting it into free atomic oxygen whereby physical and chemical changes occur, which either result in a physiological junction of the processes of the intercalary neurones by amœboid movement and multiple contacts with the processes of the first type of neurones, or a process of combustion occurs whereby the sugar is converted into energy, which serves as a source of stimulus to the next system of neurones.

Whatever it be, it is significant that these intercalary neurones should exist in well-defined layers and in such abundance in cortical situations where radiating and association tracts of fibres are ending, *e.g.*, the calcarine region where there is a double layer of granules.

Again, the great abundance of granules in the cerebellum is very significant for the following reasons :

The cerebellum is an organ of uniform structure ; it is present in all mammals. In fast-swimming fishes and mammals, *e.g.*, seals and sea-lions, it is very large ; it is very large in all fast-flying birds, especially birds of prey. This biological fact, together with the results of experiments on animals and clinico-anatomical observations in man, shows that this portion of the brain is an organ of reinforcement of muscular action, and continuous tonic contraction of the muscles depends upon its functional activity. Under the influence of stimuli from the skin, especially the soles of the feet and all the structures of locomotion, the eyes and particularly the semicircular canals, a continuous discharge of neural energy along the rubro-spinal and vestibulo-spinal tracts takes place, reinforcing with varying degrees of intensity as required the discharge from the spinal motor neurones to the muscles. It has been shown by Luciani that removal of the cerebellum in animals causes atonia, asthenia, astasia and ataxia. The layer of granules which form such a striking feature of the cerebellum may be assumed to provide an abundance of catalase for the conversion of the molecular oxygen into atomic oxygen and thus effect a continuous flow of neural energy. These and other considerations show that the oxidation processes necessary for neural activity take place at the junction of the intercalary neurones with the neurones of the first type. It is here that delay occurs in the transmission of a stimulus along a system of neurones. It may be assumed that either the chemical changes connected with oxidation are transformed into a physical stimulus, which travels along the next neuron of the first type, or the oxidation processes cause either an alteration of the surface tension or an amoeboid movement whereby a physiological junction is effected at the synapse so that the original impulse can be transmitted. The extent, character and intensity of the stimulus and its motor reaction are largely dependent upon the biological quality of the stimulus, for groups and systems of neurones are attuned by an instinctive memory or bio-rhythm to react to a biological stimulus with a specific rhythm with maximum intensity, but owing to the fact that a system of neurones with a special function is attuned to a specific bio-rhythm, a stimulus of any kind will give rise to a specific effect. This fact is proved by a simple experiment. A faradic current applied to the skin causes an uncomfortable vibration sensation ; applied to the tongue, a taste sensation ; to the eyeball, a sensation of light ; to the drum of the ear an ill-defined auditory sensation. So that owing to this inherent specific bio-rhythm of the special sense-neurones the same stimulus produces the specific effect. It may be presumed that a common mode of motion has been transformed to a special mode of motion.

Oxidation processes do not take place in a nerve, and it is incapable of fatigue. The nervous impulse as it travels along the axon is a physical disturbance unattended by any chemical change, but when the impulse reaches the terminal brush of fibrils in the grey matter it may be assumed that it liberates a catalase and oxidation processes occur.

NISSL GRANULES AN ARTEFACT, BUT THEIR PRESENCE OR ABSENCE
IN DEAD CELLS OF GREAT SIGNIFICANCE.

The living nerve-cell does not contain Nissl granules but a number of minute oval or spherical granules, which, if they escape from the cell, remain discrete. By dark-ground illumination they reflect the light and appear white; by direct illumination they appear dark and very much like an emulsion. When the cell dies these disappear, and if certain fixing reagents, such as alcohol, formol or sublimate solution be employed, a coagulation of the proteid constituents of the cytoplasm occurs causing the formation of the Nissl granules. These granules, as shown by their staining reaction with basic dye, consist of a basophil nucleo-proteid substance.

SIGNIFICANCE OF THE DISAPPEARANCE OF NISSL GRANULES.

The cytoplasm of all nerve cells contains this basophil substance, and inasmuch as it diminishes in amount or even disappears in exhausted cells it has been supposed to be the energy substance of the cell—hence has been termed “kinetoplasm.” Consequently, although the basophil substance does not exist in the form of Nissl granules in the living cells, yet a comparison of the histological appearances, as to its distribution and amount in normal cells, with the appearances presented by similar cells in morbid conditions, affords a reliable method of determining functional or organic changes of the neurones.

The Nissl granules are especially abundant and form a tigroid pattern in the large motor and sensory cells of the stem of the brain and the spinal cord; they also exist in the Purkinjé cells, the large pyramids of the cortex, and especially are they well seen in the Betz cells. In the smaller cells they are not distinctly seen, but their cytoplasm contains basophil substance in all normal cells of Golgi type I.

Morphological changes in the cytoplasm as regards the amount, distribution and arrangement of the basophil substance (chromatolysis) may therefore be correlated with disease and functional disorders of particular systems and communities of neurons having specialised functions.

Still more important are biochemical changes indicated by an

alteration in the staining reactions of the cell, for they may point to a morbid state or to the death of the cell. Whereas the morphological change previously referred to leads to depression or *suspension* of function, a biochemical change indicates a *suppression* of function. If polychrome or toluidin blue and eosin dyes be employed for staining sections we may obtain a basophil and acidophil reaction; thus a motor cell which has undergone a death-change, *e.g.*, from experimental anæmia or hyperpyrexia, stains a diffuse dull purple, the processes as well as the body of the cell having a homogeneous instead of a differential reaction to the dyes (*vide* Plate X).

Macallum has shown that the Nissl granules contain both iron and phosphorus; the basophil substance is therefore a nucleo-proteid, and, as I pointed out in my Croonian Lectures in 1900, diminution of this substance may be "an expression of the diminution of the vital interaction of the highly phosphorised nucleus upon the cytoplasm."

The abundance of nucleo-proteid, with its important iron, calcium and phosphorus constituents in the cytoplasm of the large multipolar motor cells, may be correlated with a greater potentiality for chemico-physical changes in large cells with large and relatively long axons.

The small intercalary neurones (second type of Golgi) have little or no basophil substance in the cytoplasm; the nucleus is relatively very large, but we have seen that these cells enter into the synapse of neurones of the first type.

LIPOID GRANULES IN THE CELL AND THEIR SIGNIFICANCE.

In healthy young animals lipoid granules are not seen in the cytoplasm of the neurones; they are found normally in the cells of old animals. These granules are also found in varying amount in the cells of the brain and spinal cord of human beings dying of various diseases. Thus I have found them in abundance in myasthenia gravis, to a slight degree in death from shock caused by compound comminuted fracture of the thigh from gunshot wound. They are found in old people dying of various diseases, but I have found them especially abundant and universal in the brains of cases of dementia senilis, general paralysis, dementia præcox and amaurotic idiocy. That these are not due to *post-mortem* autolytic processes is shown by the fact that these fatty granules can be seen in the perivascular sheaths and the cells of the choroid plexus. The changes observed in dementia præcox, moreover, resemble those observed in simple senile dementia (*vide* Plate XI, fig. 2).

Pighini has made a special study of the cause of their appearance, and has shown that if pieces of the brain of a healthy dog are kept in Locke's fluid in a warm chamber for twenty-four hours, these granules appear and increase in number with the length of time the tissue is kept

under these conditions. Controls showed that these were not present in the tissue before they were placed under these conditions.

The facts seem to show that up to a certain point the presence of these lipoid granules may be within physiological limits and be only a sign of deficient metabolism, incidental to a failure of complete oxidation processes, and their existence, therefore, is not inconsistent with a normal, although probably lowered, functional activity of the neurones so affected. But when the cytoplasm of a large number of cells contains abundance of these granules the physiological limit has been passed, and they are an indication of a pathological condition associated with a depression of function sufficient to give rise to impairment or even cessation of function. In amaurotic idiocy the whole of the neurones throughout the cell-body are filled with scarlet-stained globules. In dementia præcox the cells of the cortex, the basal ganglia, and the medulla exhibit this change. Especially does the process affect the cells of the frontal lobes (*vide* Plate I). Pighini concludes that these fat granules are unsaturated phosphatides, for they yield a blue-violet colour with Nile blue sulphate.

These granules stain red with Sudan III, and according to Pighini this would indicate a participation of cholesterin or of its esters with cerebroside. The tendency of the granules to stain a violet-blue colour with Nile blue also suggests the presence of cholesterin. He believed that Marinesco and Obersteiner were correct in considering that these lipoid granules in the nerve-cells of old people are products of regressive metabolism, and that hypo-oxidation and pathological processes in which katabolism exceeded anabolism would account for their occurrence; they are probably therefore an expression of anabolic hypofunction.

Having thus considered in detail certain anatomical and physiological facts concerning normal neural structure and function, we are prepared to estimate the significance of the morbid changes observed in dementia præcox, and see how far they would account for the fundamental disorders of the mind in this disease. I will commence the subject with a brief reference to the supposed causes.

THE FUNDAMENTAL MENTAL DISORDERS OF DEMENTIA PRÆCOX.

Kraepelin accepts Bleuler's distinction of *fundamental disorders* and *accompanying phenomena* of the disease. *The fundamental disorders* are those which occur in dementia simplex and in the terminal state of *simple weak-mindedness*. From this point of view the weakening of judgment, attention, of mental activity and of creative ability, the dulling of emotional interest and the loss of energy, lastly the loosening of the inner unity of the psychic life, would constitute the fundamental

disorders, while all the remaining morbid symptoms, especially hallucinations and delusions, but also the state of excitement, depression and stupor, further the manifold disorders of volition, negativism, automatism, stereotypy, automatic obedience, mannerisms, grimacing, outbursts of meaningless laughter, etc., would be regarded as secondary *accompanying phenomena* due to disruption of harmonious psychic interconnections by the degenerative process affecting functional systems of neurones in varying degrees of severity.

HISTOLOGICAL MORBID CHANGES IN DEMENTIA PRÆCOX AS DESCRIBED BY VARIOUS AUTHORS.

Histological investigations hitherto, with the exception of the examination in a few isolated cases of the sexual organs, have been devoted to the central nervous system, especially the cerebral cortex.

Macroscopically the brain and the spinal cord in these cases show little evidence of any disease.

Microscopic investigations by numerous neuro-pathologists, notably Nissl, Alzheimer, Duston, and workers (Rae Gibson and Harper Smith) in my own laboratory, have arrived, broadly speaking, at similar results.

Kraepelin sums up the changes thus :

"Nissl, in the cases of chronic evolution, has noted profound modification of the cells, which he has described under the name 'destruction of the nucleus.' A considerable number of cells appeared to be destroyed, but there is no atrophy of the cortex. The deep layers contain numerous and large neuroglial cells."

Alzheimer, studying histological lesions in acute cases of catatonia, has described grave alterations of the cells of the cortex, especially of the deep layers, notably swelling of the nuclei, infolding of their membrane, the cellular body retracted and on the way to destruction, and neoformation of neuroglial fibrils which surround the cells.

In the old chronic cases Alzheimer found wide-spread changes in the cells, which may be regarded as the terminal state of grave disease which has run its course, in particular sclerotic forms. Very frequently deposits of lipid products of decomposition were found in the various cells, even in quite young persons. Strikingly frequent were groups of nerve-cells in which the basal processes appeared to be swollen and deformed by accumulation of fat. Lastly, diffuse loss of cortical cells could be observed. These severe morbid changes affected especially the second and third cortical layers.

The observations of Klippel and L'Hermitte have shown that these primary degenerative changes of the neurones may affect the whole central nervous system, and they consider that they are either due to

an inborn biochemical deficiency, or to the effects of an autotoxin circulating in the blood after the reproductive organs have arrived or should have arrived at maturity.

All investigators refer to glia-cell proliferation. Alzheimer, in acute cases, describes amœboid hyperplasia of neuroglia, accumulation of glia-cells round the nerve-cells, and morbid new formation of fibres which surround the cells in a particular manner. Nearly all authors refer to the large swollen pale nuclei of the glia-cells, many of which can be seen adherent to, or even penetrating into, the decaying nerve-cells.

None of the authors refer to the change in the granule layers.

The histological investigations of the central nervous system in dementia præcox of all these eminent authorities are in agreement on certain fundamental points, *viz.*, that there is a parenchymatous degeneration of the neurones, and that the affections of the mesodermic vascular and supporting tissues are slight and of little importance, contrasting, therefore, most distinctly with the meningo-encephalitis of dementia paralytica and sleeping-sickness, both of which are due to a parasitic infection of the central nervous system.

The results of these observers clearly point to a primary parenchymatous degenerative process of the neurones and are in favour of the unicist conception of Kraepelin.

SUMMARY OF PERSONAL HISTOLOGICAL OBSERVATIONS.

None of the ten cases examined showed any thickening of membranes or obvious naked-eye change of the brain, in that respect contrasting plainly with dementia paralytica. Five of the cases died in pre-war times. Paraffin block-sections of various portions of the brains were prepared of 5 or 10 μ in thickness, stained by polychrome methylene-blue or methylene-blue and eosin. The remaining three were cases that have died within the last year or two. In these the brain was systematically examined both by paraffin block sections, stained in the same way as above, and frozen sections of formol-hardened material stained with Scharlach and Nile blue for lipoid granules.

The sections which had been prepared in pre-war days had retained their colour, and the results of the histological examination of these sections appended to the clinical notes of each conform, so far as they go, with results obtained in the recent cases.

Broadly speaking, the morphological changes correspond with those described by the previously-mentioned authorities. They confirm the results obtained by Klippel and L'Hermitte regarding the extension of the degenerative cell-changes to the whole brain, including in two cases

the cerebellum. They also show that there are two types: (1) In which there has been a congenital arrest of many neurones, especially of the small and medium-sized pyramids in the frontal lobe (amentia, admirably described many years ago by Shaw Bolton), and in which later at puberty or adolescence a wide-spread neuronc degeneration occurs. (2) The degenerative cell process is not associated with any congenital or prepubertal arrest of development.

The glia cell proliferation is general, and occurs especially in regions where the cell degenerative process is most marked. The neuroglia nuclei are pale in colour and seen in groups around the degenerated cells, sticking to them or penetrating the cytoplasm. I could see no spider-cells, and only slight evidence of neuroglia fibril formation by Ranke's Victorian blue stain, so characteristic of general paralysis.

The vessels show no changes: there is no perivascular-cell infiltration, nor endothelial proliferation of the capillaries, so characteristic of the meningo-encephalitis of dementia paralytica. Around the small vessels and in the endothelial cells, especially of the frontal lobe, fatty lipid granules are found (see Plate I).

There is little evidence of nerve-fibre atrophy, and sections of the brain stained by the Weigert-Pal method would afford but little explanation of the dementia. Such fibre atrophy or deficiency as occurs can be explained by the destructive decay of the cortical cells or the congenital cell deficiency. The fibre deficiency or atrophy is most apparent in the frontal lobes.

But the amount of fibre atrophy, due to cell destruction in those cases in which the demential symptoms came on first at puberty or in early adolescence, does not show a correspondence as in dementia paralytica. That being the case, we must assign the major part of the fundamental symptoms of dementia præcox to the functionally incapacitated or degenerated neurones. By this I mean the greater part of the neurones are living, but so biochemically altered that a progressive disorder and loss of function results.

My observations show that, besides the morphological changes in the cells affecting the nucleus and the cytoplasm of the cells, which have been described as occurring in the cortex by all the before-mentioned authors, there are, in addition, similar, though not as intense, morphological changes in the basal ganglia, the stem of the brain, the medulla oblongata and in severe cases of the cerebellum, but the cortical cells are most affected.

No author has paid attention, so far as I can find, to the marked nuclear and cytoplasmic changes in the layers of granules (intercalary neurones) of those regions of the cortex where these cells are so aggregated that they can easily be differentiated from the scattered pale nuclei of the neuroglia cells.

The swelling of the nucleus and infolding of the membrane of great numbers of the cells in the cortex, and to a less degree in the other regions of the brain mentioned, are well established, but no author has pointed out that numbers of the nuclei of these cells show, in varying degrees of intensity, a bio-chemical change by the fact that the nucleoli, which in normal cells are stained a deep blue (basichromatin) reaction, are stained purple or even reddish pink (oxychromatin reaction). According to Heidenhain this oxychromatin colour with eosin and blue dyes signifies a diminution of organic phosphorus (see Plates). This diminution of organic phosphorus may be associated with diminished function in relation to oxidation processes.

Besides the bio-chemical and morphological changes of the nucleus there are morphological and bio-chemical changes observable in the cytoplasm and its processes. Under a low-power magnification the cortical cells, especially the small and medium-sized pyramids, are seen to have their processes broken off, and the regular linear arrangement into the columns of Meynert may be more or less destroyed according to the advance of the disease.

There may in some cases, owing to congenital deficiency, be small places where the cells are absent. Examined with an oil-immersion normal Nissl granules are seldom seen, even in the large Betz cells or cells of the optic thalamus, corpus striatum, pons and medulla oblongata, but they are seen fairly normal in the anterior horns of the spinal cord.

Generally speaking, the Nissl pattern is not seen in the cells and dendrons, but the cytoplasm and processes are stained a dull, diffuse bluish purple and scattered throughout are vacuoles. These vacuoles are caused by lipoid granules, which have been dissolved out in the process of preparation of the sections (see Plates III and V). The cells of the inferior cervical sympathetic ganglion from a recent fatal case of dementia præcox showed abundant lipoid granules, so that it is probable that this change may be more or less universal in the nervous system in well-marked cases of this disease. As can be seen, frozen sections stained by Scharlach or Nile blue show the cytoplasm more or less filled with fat-granules (see Plate I). I have already given reasons for supposing that the basophil substance, which is the antecedent of the Nissl granules, is a product of the vital action of the nucleus on the cytoplasm, and the lipoid granules are evidence of hypofunction, which, when they are abundant and affect many cells, may be regarded as a pathological process. So that the cells in all the regions mentioned, in all the cases more or less, exhibit direct evidence of hypofunction.

No author hitherto has directly investigated the condition of the intercalary cells, although reasons have been given for supposing that

they play an important part in the formation of the synapse in all systems of neurones and in the cerebellum. Microscopic examination with an oil-immersion of regions of the cortex in which these cells form definite layers visible with a very low magnification, *e.g.*, the ascending parietal or occipital convolutions in the region of the line of Gennari and other areas, shows that these cells are profoundly modified. The nucleus is swollen with pale blue or purple staining, and often pink—indications of a bio-chemical change. The cytoplasm is hardly visible in these stellate neurones of the plexiform (the term used by Cajal and Campbell for the granular layer) layer owing to the swelling of the nucleus; fine vacuoles are, however, seen in it, and when these cells are stained for lipoid fine orange-coloured granules are observed in the cytoplasm corresponding to the vacuoles.

Similarly in these cells this reaction constitutes evidence of a hypo-function and deficient oxidation. Having this in mind I felt it would be desirable to see if this failing of the basophil substance could be demonstrable to the naked eye. I took, therefore, three pieces of tissue from three separate brains that had been hardened in formol. I selected the cerebellum because its structure is uniform, and therefore comparisons would be more reliable.

Portions of the cortex of the lateral lobe of a case of tetanus, a case of senile dementia, which showed by the usual staining methods marked changes similar but more extensive than dementia præcox, and a case of dementia præcox were taken. These were washed free of formalin and simultaneously passed through the various processes for blocking in paraffin. The three pieces in one block were cut simultaneously, the sections containing the three tissues were placed on cover-glasses, stained and mounted, so that the conditions in no way varied for each section. The granules of the tetanus case were stained much deeper blue than were the sections of the brains of the two cases of dementia. There is a possible fallacy in the fact that the length of time and the fixing fluid were not the same.

This observation, in conjunction with the previous microscopic observations, points to a deficiency of basophil substance and a diminution of the organic phosphorus in the cells of the brain of dementia præcox—a fact which may be correlated with the evidence of a failure of nuclear phosphorus in the reproductive organs. Further observations by chemical analysis of the cerebellum in dementia præcox and normal are in progress.

METABOLISM IN DEMENTIA PRÆCOX.

Pighini has carefully studied metabolism in dementia præcox. He gives the following summary of his results:

“With a view of throwing light on the metabolic change associated

with the profound symptoms of dementia præcox, I have selected four typical cases of the disease in the acute and eight in the more advanced stage, and in them I have studied the various food elements by means of numerous analyses of the food administered and the excretions. Each case gave results of interest, which may be summarised as follows :

"(1) In the dementia præcox of Kraepelin the acute phase and the advanced phase each present different modifications of altered metabolism.

"(2) In the acute phase, as evidenced by motor restlessness, sitophobia, violent impulsiveness, slight elevation of temperature, etc., there is a negative balance (increased excretion) of nitrogen (urea, uric acid, xanthin bases) of phosphorus and sulphur, indicative of a marked dissolution of the phosphorised and sulphurised proteids of the organism.

"(3) In the advanced phase, as evinced by dementia, negativism, tics, grimaces, katatonia, etc., there is a proportionate retention of phosphorus and nitrogen, a loss of sulphur proportionate to these elements, and an independent loss of calcium.

"(4) In the two phases investigated there is an altered water metabolism and a relaxed excretion of chlorine."

The great difficulties attending chemical analyses of the brain and the many sources of error in estimating metabolism in this class of patients make one careful in drawing conclusions. Still, such evidence as exists supports the view that there is a deficiency in the oxidation processes in the brain. Seeing that the microscopic investigations related tend to prove that the oxidation processes are deficient, these findings support the general premises deduced.

THE CORRELATION OF THE MORPHOLOGICAL MICRO-CHEMICAL AND CHEMICAL INVESTIGATION OF THE BRAIN AND REPRODUCTIVE ORGANS WITH THE FUNDAMENTAL CLINICAL SYMPTOMS.

A certain number of cases of dementia præcox occur in congenital aments or imbeciles. These might be termed "dementia præcossissima," and from early childhood there are clinical indications of a failure of the higher neural functions. It is quite probable that not only the brain is affected by a developmental deficiency, but that there is a general deficiency of the *elan vitale* (vital impulse), and this is manifested by the reproductive organs at puberty, which either fail to develop, or an early arrest of spermatogenesis occurs. In this connection it is interesting to note that I have shown a complete arrest of development of spermatogenesis in several cases of imbecility, also a regressive atrophy and failure of development.

Cases in which clinical symptoms first manifest themselves at puberty

or early adolescence exhibit a progressive failure of the *élan vitale*, which may be correlated with the regressive atrophy of the testes and ovaries—organs in which it can be easily demonstrated that productive energy is most active. But the active nuclear proliferation continually going on in the testes and ovaries is a synthetic process requiring active oxidation processes to build up a complex organic phosphorus compound, protamin nucleinate, out of simple phosphorised lipoid substances. The fact that these synthetic processes rapidly fail points to a germinal defect.

There is also evidence of germinal defect in the brain, for many cases of dementia præcox are congenital aments, as shown by the fact that a number of the higher cortical neurones do not develop.

The fundamental clinical disorders of dementia præcox are a weakening of judgment, of attention, of mental activity, and of creative ability, dulling of emotional interest and loss of energy; lastly, a loosening of the inner unity of the psychic life. Now if we assume that the neuron changes show (1) a progressive *suspension* of function of some neurones associated with (2) such intense bio-chemical and morphological changes in other neurones as to indicate *suppression* of function, we are able to explain remission or partial remission of some of the symptoms and sudden changes from stupor to impulsive behaviour.

Suspension of neuron function due to hypofunction from defective oxidation processes or caused by auto- or hetero-toxic conditions may vary in intensity and degree, but *suppression* of function owing to germinal lack of durability is incapable of any remission, but is progressive, so that even when a remission of some of the symptoms occurs there is a residuum of weak-mindedness—*dementia simplex*—which is progressive and continuous. It should be mentioned that the neurones are in the normal individual permanent cells adapted for a prolonged life, and protected by special anatomical conditions from injury and disease. Any form of stress, using the term in the wide sense employed by Mercier, will contribute to lower the durability of the neurones.

Now it is known that some cases which at first clinically appear to be cases of dementia præcox recover. But some cases of confusional insanity may present a clinical picture of dementia præcox and recover completely. It must be supposed that these cases are due to a hypofunction, and we should probably find a general condition of lipoid granules in the neurones, with basophil chromatolysis and disappearance, or partial disappearance, of the Nissl granules.

But evidence of a biochemical and morphological degeneration of the nucleus points to a condition which would end in suppression of function, although this condition does not necessarily imply death of the neurone and atrophy of the axon. The morphological changes

implying *suppression* of function are found especially in the cortex, and particularly the cortex of the frontal lobes, in which neuroglia proliferation is most marked. Associated with this are universal changes in the various regions of the brain pointing to hypofunction, *viz.*, lipoid granules in the cytoplasm, and in many cells an oxychromatin, or a tendency to an oxychromatin reaction of the nucleus.

The affection of the stellate intercalary cells which enter into the synapse, and the evidence I have adduced of the importance of these cells in connection with oxidation processes productive of neural energy and transmission of nervous impulses, suggest that a hypofunction or suspension of function of these neurones would lead to synaptic dissociation, and thereby account for psychic dissociation and the coming and going of symptoms; or where there is a permanent morbid change, to a suppression of their function with permanent dissociation.

We have thus two morphological conditions which will account for the fundamental disorders, and the nature of these disorders will depend upon the cerebral structures affected, whether in such a way as to produce suppression or suspension of function. Naturally the nature of the mental disorders will also depend upon the localisation and the relative intensity of the hypofunction, suspension, or suppression of function of the neurones.

It is quite probable that there is a hypofunction of the whole of the bodily tissues, especially of the reproductive and endocrine systems, and associated with deficient oxidation processes; there is certainly a diminished vital resistance to microbial infections. A large percentage of these cases of dementia præcox die of tuberculosis, but my observations show that exactly the same neuronic changes can be found in dementia præcox cases that have died of acute pneumonia. So that although it is common to find stupor in patients affected with active tuberculosis, and although the absorption of toxins may therefore have played a part in the production of some of the symptoms, yet I have formed the conclusion that the essential cause of this disease is an inborn germinal defect.

In conclusion I would like to express to you my grateful acknowledgments for so kindly listening to an account of my investigations upon an extremely difficult subject, for I feel that it is one which still requires an enormous amount of patient research before definite conclusions can be arrived at, and the more I work at this subject I am convinced of the wisdom of following the advice of Francis Bacon in his *Advancement of Learning, Divine and Human*, when he says: therefore in this, as in all things practical, we ought to cast up our account, what is in our power and what not; for the one may be dealt with by way of alteration, and the other by way of application."

MAUDSLEY LECTURE.¹

By SIR FREDERICK MOTT, K.B.E., M.D., LL.D., F.R.S.

Delivered at the Quarterly Meeting of the Medico-Psychological Association of Great Britain and Ireland, held at the Maudsley Hospital, Denmark Hill, S.E. 5, on Tuesday, June 7th, 1921.

MR. PRESIDENT AND MEMBERS OF THE MEDICO-PSYCHOLOGICAL SOCIETY,—Permit me to thank you for the great honour you have conferred upon me in asking me to give the second Maudsley Lecture; also for permitting me to deliver it in the Hospital which bears his illustrious name and which owes its existence to his generosity.

I propose to divide this address into two parts: the first will treat of the hospital, its inception and its aims and uses as conceived by the founder; the second part will deal with researches I have carried on concerning dementia præcox.

I.

THE MAUDSLEY HOSPITAL, PAST AND PRESENT.

It is now fourteen years since the late Dr. Henry Maudsley wrote me a letter saying he would give £30,000 to the London County Council if they would build a hospital in London for the study and investigation of mental disorders in their early stage, and the treatment of such with a view to preventing them being sent to the county asylums. The County Council acknowledged Dr. Maudsley's very generous offer, and the conditions upon which the gift would be made were drawn up by Dr. Maudsley and myself. They were that the hospital should be built within four miles of Charing Cross and be associated with the London University.

Dr. Maudsley recognised that the best and only method for providing means for the cure and prevention of insanity was by the encouragement of clinical and laboratory research, and he conceived the idea that a hospital with 100 beds and out-patient departments would enable a careful study to be made of cases of incipient mental disease, and if connected with the University it would become a centre for post-graduate teaching.

In 1907 I visited Kraepelin's clinic at Munich, and having long been acquainted with the remarkable clinical and anatomical research work which he and Alzheimer had carried on there, and knowing the

¹ Reprinted from the 'Journal of Mental Science,' July, 1921.

influence this school had had upon psychiatry in the whole civilised world and Germany in particular, I was not surprised to find that this clinic attracted students and doctors interested in the study of mental diseases from all countries. There was no such hospital and clinic in England, and in the preface of the third volume of the *Archives of Neurology* (1907) I expressed the following opinions:

"A fruitful field of study in psychiatry would be those early cases of uncertifiable mental affection termed neurasthenia, psychasthenia with obsessions, mild impulsive mania, melancholia, hysteria and hypochondria, which in many instances are really the prodromal stages of a pronounced and permanent mental disorder. The poorer patients suffering with these conditions first come into the hands of the practitioner, the dispensary or infirmary doctor, and the out-patient physician at the general or special hospitals. The better-class patients are sent by the practitioner to the neurologist; the generality of the poorer patients, and sometimes the better-class patients, are regarded by the medical man who has had no training in psychology as of little medical interest (for such patients do not, as a rule, benefit by drugs), and he finds it a wearisome task to listen to their story, to ascertain their inborn tendencies, and to find out the truth of what has happened to account for their strange conduct indicative of their not feeling, thinking and acting in accordance with the general usages of their social surroundings, and yet such patients may not be so antisocial as to be certifiable. Such cases are often in the hopeful and curable stage, and these, if studied carefully by trained medico-psychologists, could not fail to yield valuable results in regard to our knowledge of the causation, prevention and cure of insanity. Moreover, when the cases are followed up systematically they would throw much light on prognosis in similar cases. The majority of cases which are admitted to the asylum have long passed the hopeful stage; still, there are a certain number of early curable cases, and these, I maintain, would sometimes be much better if they had not been certified or sent to associate with chronic lunatics. Fortunate would be the community in which there was a fully-equipped and well-organised psychiatric clinic, under the control of a University, and dedicated to the solution of such problems. If suitable post-graduate training in medico-psychology and neuropathology were established, doubtless the Universities and licensing bodies might be induced to establish a diploma, very much on the lines of the Diploma of Public Health, which has largely contributed to raise the science of public health to the high position it now holds, thus conferring an inestimable benefit on the nation."

Shortly after this was published Dr. Maudsley called upon me but I was out, and he wrote me a letter saying that he would give £30,000

to the London County Council if they would build a hospital in London for the study and treatment of acute mental disorders. I interviewed Sir John MacDougall, who advised me to represent to Dr. Maudsley the desirability of making his gift subject to an association of the hospital with the London University.

In March, 1908, the Asylums' Committee reported as follows: "We desire to express for our own part the appreciation of the generous spirit in which Dr. Maudsley's offer has been made, and our conviction that its acceptance will confer a great and lasting benefit upon a class of sufferers, the effectual assistance of whom has hitherto been amongst the most difficult of social problems."

The offer was accepted by the Council, but for some years both Dr. Maudsley and I were almost in despair as to whether the Council would ever find a suitable site. At last, in 1912, the present site was purchased for £10,000, and plans were drawn up by Mr. Clifford Smith, the asylums' architect and engineer, in which I co-operated. A building strike occurred, and owing to the delay the cost of the building was increased by 25 *per cent.*

The hospital was only partially completed when the war broke out. King's College Hospital and the adjacent schools formed the 4th London General Territorial Hospital, upon the staff of which I served in the rank at first of Major, afterwards as Brevet Lieut.-Colonel, as neurological specialist. To this hospital was sent a large proportion of neurological cases; consequently I suggested to the War Office authorities that if the Maudsley Hospital was completed it would form a very useful addition, and be particularly valuable for the treatment of the more serious cases of war psychoneuroses and psychoses.

Sir Alfred Keogh, D.G., inspected and approved of the hospital, which was completed at the end of 1915, and opened for patients early in 1916 as a part of the 4th London General Hospital.

The Pathological Laboratory at Claybury was dismantled and the equipment transferred to the more convenient and spacious laboratory at the Maudsley Hospital.

I had frequent opportunities of talking over the progress of the building operations, and, when completed and open for the reception of neurological cases, of discussing with Dr. Maudsley the clinical and pathological work that was being carried on there, in all of which he took a great interest.

The Maudsley Hospital now had become widely known, and successive groups of American officers were sent here for training before proceeding abroad. Several distinguished foreigners who were driven from their country were enabled by grants from the Medical Research Council to work in the laboratory. Thus Dr. Sano, formerly the superintendent of the Acute Mental Hospital, Antwerp, and now the

Superintendent at Gheel Colony, pursued valuable researches on "The Convolutional Pattern of the Brain in Identical Twins," published in the *Philosophical Transactions of the Royal Society*; "The Convolutional Pattern of the Brain in Fifteen Pairs of near Relatives," published in the seventh volume of the *Archives of Neurology and Psychiatry*, and "The Description of the Brain of the Idiot Savant of Earlswood," published in the *Journal of Mental Science*. Prof. Marinesco, the distinguished neurologist of Bucharest, investigated "The Histology of Lethargic Encephalitis," "The Oxidase Reaction of the Central Nervous System," and "The Histology of Painful Neuromata in Amputation Stumps," which was published in the *Philosophical Transactions of the Royal Society*.

From the early part of 1915 and onwards I made researches on the brains of cases sent to me from France in connection with the effects of high explosives and gas poisoning, which formed the subject of the Lettsomian Lectures of 1916 and subsequent publications in vol. vii, *Archives of Neurology and Psychiatry*.

The clinical and pathological work which was being carried on here was much appreciated by Dr. Maudsley, and this was shown by a letter which I received from him in July, 1916, in which he says: "I have had two or three casual reports of all that the hospital is doing from visitors, who were very pleased. In getting the hospital on to right lines you are doing good pioneering work which cannot fail to have its reward, and it will depend, as you know I think, on you to make it what it should be; 'therefore be not weary in well doing.'"

Impressed by the lack of knowledge of neurology and psychology by medical officers, and especially in the diagnosis and treatment of the war psycho-neuroses, I started classes of instruction, which were first largely attended, especially by officers from the Dominions and United States; but later, owing to the blighting hand of officialdom, these classes died of inanition. I am glad, however, that I did start these classes of instruction, for it gave me the idea that many qualified medical men were anxious to acquire a knowledge of nervous and mental diseases if suitable courses of instruction were offered to them. I must tell you that the Pathological Laboratory continued to do the routine work for the London asylums during the whole time of the war as well as the pathological work for the hospital. Moreover, a part of the laboratory was utilised for the investigation of malaria by Sergt.-Major Nierenstein, Captain Thomson, and subsequently Capt. Mann. The original work of Sergt.-Major Prof. Nierenstein, of Bristol University, was of very considerable value, and formed the subject of a report on "The Presence of Hæmo-Quinic Acid in the Urine of Cases of 'Blackwater.'"

In September, 1919, the hospital was transferred to the Ministry of

Pensions, and in April, 1920, with the approval and under the auspices of the L.C.C., I started classes of lectures and practical instruction for graduates of medicine, especially medical officers of asylums, to enable them to sit for the Diploma of Psychological Medicine for the University of Cambridge, which had been established just before the war. The syllabus was submitted to Sir Clifford Allbutt and Prof. Sherrington, who was one of the examiners, and received their approval; it did not quite correspond with that of the Cambridge University. An announcement was made in the journals that this course would be given with a view to preparation for qualified medical men who were desirous of taking the D.P.M. of the University of Cambridge. This caught the attention of the Registrar of the University of London, who wrote asking me if there was not a University of London. My reply was "Yes, but there is no diploma." The Royal Colleges also woke up at this eleventh hour. I may say that thirteen years ago I approached the President of the Royal College of Physicians urging him to support the establishment of a diploma in psychological medicine, but without effect. Possibly the lack of knowledge of neurology and psychological medicine of medical men serving in the Army and on the Pensions' Board and the very serious results which occurred in consequence, both during and after the war, opened the eyes of many of the distinguished heads of the profession who had served in the Army.

Now at last, after thirteen years, I have seen my wishes fulfilled by the establishment of a D.P.M. in more than one University and by the Royal Colleges. I agree with the Medical Correspondent in the *Times*, that attendance at lectures and practical instruction in neurology and psychology for the first part of the Examination for the Diploma, and attendance at the lectures and practical instruction in nervous and mental diseases for the second part of the Examination, is the best corrective to the growth of a superficial and spurious form of psychology which appeals to a certain class of people, whose minds are open to any suggestive influence, and who are ever ready to run after any new craze, good or bad. To such people psycho-analysis appeals. If only this mode of treatment remained in the hands of properly trained medical men well qualified by their personality, their study, knowledge and experience of the character and conduct of their fellow human beings, enabling them to handle the problems of the sexual instinct and its latent manifestations with delicacy and care, it would not matter; but unfortunately it is getting into the hands of undesirable and unqualified persons.

Since the Laboratory has been under the Ministry of Pensions a number of men have been doing research work here, notably Dr. Golla who is giving the Croonian Lectures this year on "The Objective Study of Neurosis," the following Japanese gentlemen, Dr. Matsu-

moto, Dr. Morowoka, Dr. Hayao, Dr. Uno, Dr. Kominami, and their work will be published shortly; also Mr. Kenneth Walker and Dr. Prado y Such. I mention all these names because it shows that active research has been done, although the Hospital has had no patients since November 1st, 1920. Unfortunately there is no likelihood of the hospital being opened for the purpose for which Dr. Maudsley made his generous gift for some time to come; consequently a research which I had contemplated on metabolism in dementia præcox, and for which the Board of Control gave me a grant, cannot be carried on.

It will thus be seen that the hospital has fulfilled two out of the three wishes of Dr. Maudsley, namely—practical instruction and lectures in psychological medicine have been given for more than a year. The classes have been well attended by a number of men in the L.C.C. asylums' service and from various parts of Great Britain, and many of them have been enabled to pass the examination for the Diploma for the Universities of Cambridge, London, or that of the Conjoint Board. I have been extremely fortunate in being able to get a first-rate panel of lecturers, and I take this opportunity of thanking them for their services.

They were as follows:

Dr. Golla, who has given lectures on Physiology of the Nervous System and Practical Physiology in Part I of each of the three courses of lectures, as well as Clinical Demonstrations in Neurology in Part II of the First and Second Course.

Dr. Lowson, who gave Lectures on Psychology and Demonstrations in Practical Psychology in Part I of the First Course.

Dr. Hubert Bond, who gave lectures on the Diagnosis, Prognosis and Treatment of Mental Diseases and Demonstrations of Same and Legal Relationships of Insanity for Part II of the First and Second Course.

Sir Bryan Donkin, who gave lectures on Crime and Responsibility for Part II of the First Course.

Dr. F. C. Shruballs, who lectured and gave demonstrations of cases on the Practical Aspect of Mental Deficiency for Part II of the First and Second Course.

Dr. William MacDougall, who lectured on The Psychology of Conduct for Part II of the First Course.

Dr. Bernard Hart, who lectured on The Psychoneuroses for Part II of the First and Second Course.

Dr. W. C. Sullivan, who lectured on Crime and Insanity for Part II of the Second Course.

Dr. E. Mapother, who lectured on the Symptoms of Mental Disease for Part II of the Second Course.

Dr. Devine, who gave the lectures on Psychology and the Demon-

strations on Practical Psychology for Part I of the Second and Third Courses.

I lectured and gave practical instruction and demonstrations on The Anatomy of the Nervous System for Part I of the First, Second and Third Courses, and lectured on the Pathology of Mental Diseases, including Brain Syphilis, its Symptomatology and Treatment ; also gave Clinical Demonstrations in Neurology for Part II of the First and Second Courses.

I should particularly like here and now to express my deep sense of obligation to the Board of Control and the Medical Research Council for the generous way in which they have supported me in grants for carrying on researches in the Laboratory, and by the aid thus afforded enabling me to publish the same with proper illustrations.

Maudsley on Body and Mind.

Before commencing the second part of my address I will quote some passages from Dr. Maudsley's Goulstonian Lectures on "Body and Mind" given fifty years ago, which show that he was fully aware then of the importance of the objective study of the mind and its disorders and the inter-relation of function of body and mind :

"Mental disorders are neither more nor less than nervous disease in which mental symptoms predominate, and their entire separation from other nervous diseases has been a sad hindrance to progress. No doubt it is right that mental derangements should have, as they often require, the special appliances of an asylum, but it is certainly not right that the separation which is necessary for treatment should reach to their pathology and to the method of its study. So long as this is the case we shall labour in vain to get exact scientific ideas concerning their causation, their pathology and their treatment.

"Clearing then the question as completely as possible from the haze which metaphysics has cast around it, let us ask—How comes idiocy or insanity? What is the scientific meaning of them?"

Yet at the present day we find many authorities attributing mental disorders to psychogenic causes instead of to pathogenic conditions. It has been my endeavour to show that mental processes are subordinate to physiological processes and that mental disorders and diseases are due to pathological physiogenic conditions, and I am sure that in doing so and in encouraging research on those lines I shall be clearly following out Maudsley's wishes. In these same lectures Maudsley emphasises the importance that the generative organs have upon the mind, and he asks the question whether each of the internal organs has not also a special effect, giving rise to particular feelings with their sympathetic ideas. But this was long before our knowledge of the endocrine system ; still, he shows by his reference to the sexual

organs what an important influence they have upon the mind in health and disease, as the following passages show :

" We have indeed to note and bear in mind how often sexual ideas and feelings arise and display themselves in all sorts of insanity, and how they connect themselves with ideas which in a normal mental state have no known relation to them, so that it seems as inexplicable that a virtuous person should ever have learnt as it is distressing that she should manifest so much obscenity of thought and feeling !

" Considering, too, what an important agent in the evolution of mind the sexual feeling is, how much of thought, feeling and energy it remotely inspires, there is less cause for wonder at the naked intervention of its simple impulses, in the phenomena of mania, when co-ordination of function is abolished in its supreme centres and the mind resolved as it were into its primitive animal elements. The reciprocal influence of mind on organ and organ on mind is well illustrated in the sex organs.

" The morbid self-feeling that has its root in the sexual system is not unapt to take a religious guise."

II.

FURTHER RESEARCHES ON DEMENTIA PRÆCOX.

Throughout Maudsley's writings, which extend over fifty years, one finds that he views mind and its disorders from a broad biological aspect, and one of his sayings is : " Nature is unmindful of the individual, mindful only of the species."

Natural selection and the survival of the fittest is still going on whereby weak types are eliminated, and should the social conditions be such as to prevent this natural selection and survival of the fittest, racial decay must inevitably set in.

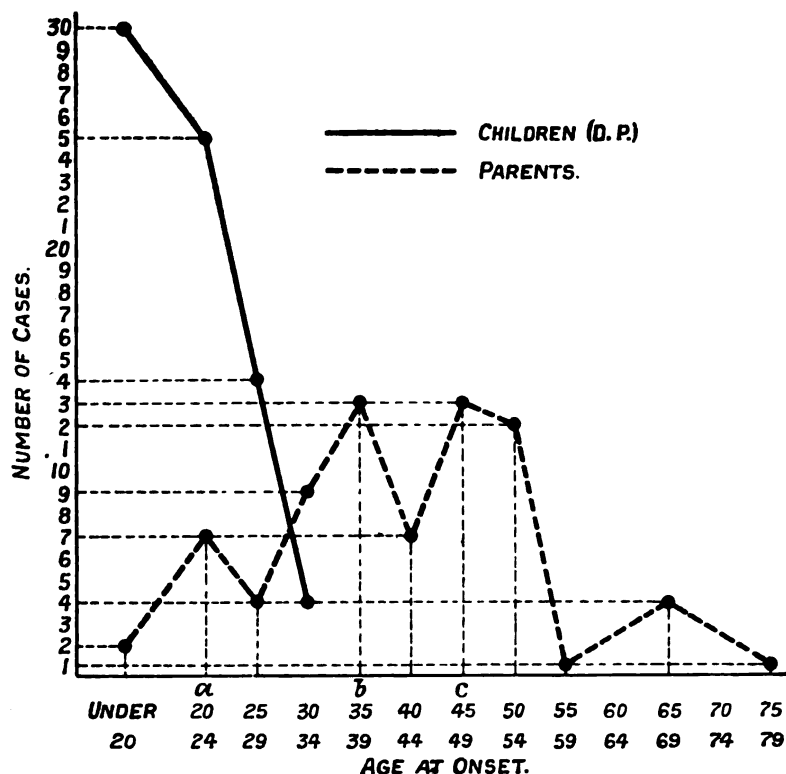
Impressed by the teaching of Morel, who in 1859 pointed out that the progressive uninterrupted transmission of a neuropathic type leads finally to special degenerative forms, to imbecility and idiocy, and with the diminished capability of production of the latter kind the stock gradually becomes extinct, Maudsley says that Nature always tends to end or mend a degenerated stock. This dictum received proof from my investigations on anticipation.

Anticipation and Survival of the Fittest.

In 1911 I published statistical data relating to the age of onset of insane offspring and of insane parents. This was based upon a card system relating to 3,118 relatives who had been admitted to the London County asylums and made up from 14,050 families. This analysis

showed a singular tendency to the occurrence of insanity at an earlier age in the offspring than in the parents.

In 1917 I made a further analysis of the relative cards since 1911—a period of six years. This analysis was limited to insane parents of offspring of which a diagnosis of dementia præcox was made. The graph is similar in its characteristics with regard to the graphs of the age of onset of the parents, but in respect to the age of onset of the offspring, instead of 47·9 *per cent.*, as in the first analysis,



The curve of the parents resembles very much the general curve of the asylum cases with three periods of greater intensity: adolescence (*a*); G. P. period (*b*); involutional period (*c*).

being under twenty-five upon admission, 75 *per cent.* of the cases suffering with dementia præcox were under the age of twenty-five on admission.

No cases of dementia præcox were among the parents, and this agrees with Rudin's investigations. Seeing that a great many cases were either insane before certification or by their conduct had given prodromal evidence of oncoming insanity, it is probable that all the cases commenced before the termination of the adolescent period of

life. This fact supports Maudsley's contention that there is a tendency to end or mend a degenerated stock. Now, how could Nature otherwise act, in ending or mending a degenerated neuropathic stock, except by bringing disease on at an early age, by which the organ of external relation, the brain, becomes diseased, and thus renders an individual so affected unable to compete with his fellows in the struggle for existence? Clearly such a condition of a disordered mind would operate by natural selection in the struggle for existence and survival of the fittest among primitive people; but among civilised people, where the struggle for existence and survival of the fittest does not eliminate poor types but rather tends to preserve them, other than natural methods must be adopted, *viz.*, segregation. Fortunately, cases of dementia præcox sooner or later become anti-social and are sent to asylums, where they are usually detained for the rest of their lives.

But my investigations on the reproductive organs of both sexes in this disease show that Nature has adopted an even more certain method of eliminating this form of degeneracy in a stock, *viz.*, by progressive regressive atrophy of the testis and ovary. In the cases of females this regressive atrophy not infrequently occurs after the first pregnancy, and all the evidence goes to show a lack of the psycho-physical energy connected with the sex instinct—an instinct which energises and dominates all the cells of the body for the purpose of the preservation of the species. This lack of psychophysical energy is one of the striking features of this disease, and it shows it both in disordered mental and bodily functions.

In my Morison Lectures and in *Studies of the Pathology of Dementia Præcox*, I have pointed out the intimate correlation of the sex organs and the endocrine system. Naturally the mental symptoms develop progressively, and show themselves first by a disintegration of the psychic unity affecting the highest of the psycho-physiological levels. It might be argued that the degeneration of the sexual organs was secondary to the mental deterioration, and that the mental deterioration was of psychogenic origin, but I have given reasons which I shall develop a little more fully later why this is not the cause.

COMPARISON OF AN ACQUIRED DISEASE (GENERAL PARALYSIS) WITH DEMENTIA PRÆCOX, AN INBORN GERMINAL DISEASE.

A comparison of the mental and bodily conditions of an acquired disease—general paralysis of the insane—with the mental and bodily conditions found in dementia præcox, will be the argument which I should advance to show that dementia præcox is a vital defect of the reproductive organs and of the brain, in particular, and probably of the whole body.

The Testes and Spermatogenesis in General Paralysis and Dementia Præcox.

If we compare the reproductive organs in general paralysis with those of dementia præcox, we shall observe that in the most advanced cases of dementia paralytica portions of the testes, sometimes the whole testes, show signs of active spermatogenesis, and this applies to general paralysis, due to congenital as well as acquired syphilis. Indeed I have found in a case of tabo-paralysis, due to congenital syphilis, live spermatozoa in the vesiculæ eight hours after death. If we compare the average weight of the testes in eighteen cases of general paralysis after removal of the tunica vaginalis and epididymis, with the average weight of the testes from a similar number of cases of dementia præcox, we shall find that in the former the average weight of the organ was 18 grm. and in the latter 12. Moreover, this is in spite of the fact that in cases of general paralysis there was evidence of chronic inflammation with adhesion of the tunica vaginalis, so that sometimes one organ was considerably atrophied. In no case did we fail to find spermatozoa in the vesicular fluid or in an emulsion of the testes in general paralysis; whereas in dementia præcox in considerably more than half the cases no evidence of spermatozoa could be found. On section of the organs in dementia præcox the spermatic tubules may appear white, owing to the lipoid contained in them, but this does not always show that the organs on microscopic examination will present normal histological appearances, for reasons which I will state later. Generally speaking, however, especially in more advanced cases and those testes weighing 12 grm. or less, the tubules to the naked eye, or when examined with a hand lens, appear attenuated and of a greyish or greyish-white colour, instead of milky white, and there is obviously in these cases an increase of interstitial tissue.

Whereas on the one hand in general paralysis, especially in organs where a number of tubules have been atrophied, owing to local specific gonorrhœal or syphilitic inflammatory reaction causing obstruction to the vasa efferentia, the hormone interstitial cells of Leydig are clearly seen upon microscopic examination; on the other hand, in dementia præcox these hormone cells are difficult to observe and sometimes impossible to find. There can be no shadow of doubt about the existence of a progressive regressive atrophy of the testes in the majority of the cases of dementia præcox. Generally the atrophy is proportional to the number of years or the early age at which the disease first became manifest; but there were a few cases in which the testes appeared to be of average weight, and in which active spermatogenesis could be found on microscopic examination and in which spermatozoa were found in the vesiculæ. I shall deal with these

in the demonstrations which I shall give at the end of the lecture when I refer more particularly to the recent researches which I have been making with Dr. Prado y Such by a special technique.

The Ovaries in General Paralysis and Dementia Præcox.

Now when we come to compare the ovaries of the cases of general paralysis with those of cases of dementia præcox the subject becomes more difficult in one way and easier in another. It becomes more difficult to estimate the respective average weights, because in most of the paralytic women who have died the process of involution of the reproductive organs has commenced.

There have been, however, a few cases of congenital syphilis causing the juvenile form, and these present a striking difference to those of cases of dementia præcox as regards the appearance of the ovaries upon section. In the former one observes maturing Graafian follicles, whereas in the latter these are not observed. In a general paralytic woman from acquired syphilis there are usually large numbers of *corpora lutea vera* whereas in dementia præcox there are relatively few, even when the disease has affected married women. On microscopic examination one seldom sees in cases of dementia præcox any evidence of primordial follicles showing any tendency to develop a zona granulosa, and still more rarely to form even the early stages of a Graafian follicle, whereas normal follicles in all stages of development may be found in cases of paralytic dementia, whether due to acquired or congenital syphilis, and in spite of long mental disease and bodily intercurrent disease of the same nature, as proved fatal in the cases of dementia præcox. As a general rule if the patient suffering with general paralysis has died before the involutional period, one finds on microscopic examination abundant evidence of maturation of the primordial follicles with the formation of atretic follicles and corpora atretica. These maturing follicles do not go on to a complete ripe Graafian follicle because of the mental and bodily disease from which the patients are suffering, and in this respect differing from the male paralytic, in which, as I have said, active living spermatozoa exist. Now this seems to prove that the acquired disease—general paralysis—has not affected the specific vital energy of the ovum, and this fact may be correlated with the fact that in the testes, even in advanced general paralysis which has lasted many years, we still find evidence of productive energy by the existence of active spermatogenesis.

Sexual Organs and Psychophysical Energy.

The question then arises: What is the cause of this failure of vital energy, and what influence has it on the body as a whole

and on the production of the mental symptoms? There is evidence to show that the organs of reproduction play an important part in regulating and controlling the functions of the endocrine system.

I have not time to develop this part of the subject, but there are many facts which support this statement; but it may be asked: What relation has this regressive atrophy of the reproductive organs which are dominant in the life of internal relation upon the central nervous system which controls all sensori-motor activities? From a broad biological standpoint it may be assumed that after puberty the psychophysical energy of the whole body is expended in response to the three primal instincts—self-preservation, propagation and the herd instinct, which last has arisen out of the first two. If sexual desire is lost one great source of psychophysical energy dries up and this must lead to an increasing development of the self-regarding sentiment, because nearly all the passions and altruistic sentiments have their roots in the instinct of propagation and the tender emotions connected with the care and nutrition of the offspring. But it may be argued that the mental symptoms precede the loss of function of the sexual glands, and therefore, while one will not admit that the pathological physiogenic conditions are secondary to the psychogenic, one cannot avoid an explanation of why the mental symptoms precede the loss of the sexual activity. The explanation, to my mind, is that in this disease there is a failure of vital energy of the cells of the whole body, manifested especially in the two most important to show symptoms, namely the closely inter-related sexual organs and the brain, and particularly in that part of the brain which constitutes the highest psycho-physiological level; the level which has been the last to come phylogenetically and ontogenetically and is the first to go. For this reason I am doubtful whether cases of dementia præcox can benefit from psycho-analysis.

Comparison of the Pathological Changes in the Nervous System in Relation to Symptoms in General Paralysis and Dementia Præcox.

It may be argued by those who are in favour of the psychogenic origin of dementia præcox that the pathological changes found in the nervous system are insufficient to account for the mental symptoms which occur in this disease. I believe that there is sufficient to account for the symptoms if we regard the disease from a physiological point of view. It is quite obvious that the gross changes which are met with in dementia paralytica, changes involving the destruction of the neural elements proportional to, and accountable for, the degree of paresis and dementia which are met with, do not exist in dementia præcox. In this disease the naked-eye appearances are those of a normal brain. There are no inflammatory changes in the vessels;

no thickening of the membranes; no wasting of the brain substance with corresponding increase of cerebro-spinal fluid such as is found in paralytica dementia. Whatever the physiogenic cause, then, it can only be found by microscopic examination.

Neural Activity Dependent upon Physiological Processes and Evidence of their Failure in Dementia Præcox.

Now, it has been known for a long time that there are microscopic changes affecting particularly the nucleus with diminution of the Nissl substance, distortion and shrinking of the cells of the brain, associated with a lipoid degeneration of the cytoplasm affecting especially the higher levels, but not limited to any part of the brain in dementia præcox (*vide* Plate X). How can we then, it may be asked, associate these anatomical findings with a disorder and loss of function of the neuronic systems to account for the symptoms? It is difficult, but there seems to me to be evidence in the decay of the nucleus of a failure in the specific vital energy of the neurons. Now what part does the nucleus play in the function of the neuron, and how is it related to the Nissl substance? The Nissl substance, as MacCallum has shown, is a nucleo-proteid containing phosphorus and iron. The Nissl granules do not exist in the living cell, but there must be this nucleo-proteid present in another form; the larger the cell the more abundant it is. This is evidence to show that this basophile staining nucleo-proteid has a specific biochemical function. We know that experiments involving fatigue cause a disappearance of the Nissl substance, which indicates that functional neuronic activity is dependent upon it. Now Marinesco has shown that upon all the processes of the dendrons and the cell body there are oxidase granules, but none on the axon. These granules consist of a lipoid substance containing an unsaturated fatty acid substance on the surface, which takes up molecular oxygen (O_2) from the blood. The iron and probably the phosphorus contained in the basophile (Nissl) substance of the cell which is also found in the dendrites, and not on the axon, would therefore act as a catalase on this molecular oxygen and convert it into free atomic oxygen ($O-O$). When the stimulus comes to the neuron it may not cause a response, but as a result of a succession of stimuli—that is, summation—the resistance in the grey matter at the synaptic junctions is overcome and the stimulus is perceived. This may be explained by the fact that an insufficiency of catalase has been formed by the first wave of stimulus to bring about changes in the synaptic junctions to enable it to pass through to the receptor centres.

Experiments and observations show that neural function depends upon the circulating blood carrying oxygen to the tissues. Thus Mosso

found that a patient who had been trephined, and in whom the pulsation of the brain could be felt, lost consciousness six seconds after the pulsation had been made to cease in consequence of compression of the carotid arteries. The blood supply of the grey matter is six times as great as that of the white matter, and there is reason to believe that all the active oxidation processes take place in the grey matter. Moreover, delay in passage of an impulse is in the grey matter. Whereas neuron fatigue occurs from over-stimulation in the cell and its dendrons, where the oxidase granules are situated and where the oxygen is essential for functional activity; experiments show that the axon, the conducting agent of a nerve-fibre, is incapable of being fatigued by stimulation even when contained in an atmosphere of nitrogen. The stimulus conducted along the axon is therefore biophysical, but in the cell and dendrons, under the influence of a stimulus, it may be assumed nuclear catalase is liberated and acts upon the oxidase granules in the grey matter, converting molecular O_2 into $O-O$, whereby a vital bio-chemical process is set up in which $O-O$ is used up and CO_2 produced. This vital process engendered by the impulse is necessary for its transmission through the synapse to the next neuron. The precise nature of this vital process we do not know; it may be of an anæboid nature, or an alteration of the surface tension at the synaptic junction. In a neuron system there are two sets of neurons in the chain—neurons of the first type of Golgi, in which the axon leaves the grey matter and is covered with myelin, and neurons of the second type in which the axon does not leave the grey matter, so that the intercalary neurons of the second type always enter into the synapse. As these consist largely of nucleus, it follows that there is abundance of catalase available at the synapse to convert the molecular oxygen into free atomic oxygen. In the cortex of the brain these intercalary neurons form definite layers of granules, and act as receptors for afferent projection systems and association systems of neurons, well exemplified by the double layer of granules in the half vision centres. Marinesco found abundant oxidase granules in this layer of granules (plexiform cells of Cajal).

If, then, we can assume that neural activity depends upon the physiological processes in the grey matter, which I have indicated, then it is a rational hypothesis to put forward that the failure of function in dementia præcox may be correlated with a failure of oxidation processes in the grey matter, owing to a deficiency of the vital energy of the nucleus, as shown by morphological and bio-chemical changes in the nucleus and a failure in the production of the substance which is the antecedent of the Nissl granules.

The lipid granules which are found in the cytoplasm in dementia præcox and senilis are an expression of a deficient metabolism of the

neuron (*vide* Plate XI). Similar appearances are found in the neurons of old people and old animals; and we may regard the change as it occurs in dementia præcox as a wide-spread loss of vitality and premature decay affecting the cells of the highest physiological levels first, but occurring at all levels. Although the neurons when so affected cannot function normally and dissociation of systems of the highest evolutionary levels occurs, the neurons are not necessarily dead, there is a suspension of function of some and suppression of function of others according to the degree of intensity of the nuclear decay. I have dealt at fuller length in the Morison Lectures upon this theory of failure of neuronic activity.

*Recent Observations on the Histology of the Testes and Ovaries in
Dementia Præcox.*

At the last meeting of this Society I gave a demonstration of the "Histological Changes in the Reproductive Organs in Health and Disease," and I pointed out that there were three or four cases of dementia præcox in which I had found active spermatogenesis and several in which the macroscopic appearances might have passed for normal. A very pertinent question was put by a member regarding these cases. Why should the testes appear normal and active spermatogenesis be found in some cases of dementia præcox if this disease is associated with a germinal deficiency causing a regressive atrophy? I replied that every case that is diagnosed clinically as dementia præcox is not necessarily a case of that disease, especially if it be a case of relatively short duration as regards mental symptoms, as these cases were. But the case in which I had the greatest difficulty to show any regressive atrophic change was one that had been diagnosed dementia præcox by a very skilled and competent authority, so that it was necessary to find another explanation, and this is the one I will offer. Every pathological process which is of a primary progressive nature must have a beginning, and the technique which I at first employed may not have been sufficiently refined to show the earliest changes. Dr. Prado y Such (a pupil of Ramon y Cajal), a worker in this laboratory, has co-operated with me in a further research to demonstrate the finer histological changes by a special silver method of staining of frozen sections of tissues impregnated with gelatine, so as to hold all the delicate structures together *in situ*. We have been able by adopting this technique to show changes in these earliest cases where there is no loss of weight of the organs and normal naked-eye appearance and further upon microscopic examination showed active spermatogenesis. Sections of the testis of a young man who died of infective endocarditis were prepared and stained by the same method for comparison.

The Various Stages of Regressive Atrophy of the Testes.

I will throw on the screen lantern-slides showing on one side the normal, on the other the three stages met with in dementia præcox (*vide* Plates II–VII). It will be observed that even in the earliest first stage a commencing regressive atrophy can be seen, for some of the tubules are beginning to shrink; there is a crinkling of the membrana propria; the tubules are not so closely approximated as in the normal and there is a corresponding increase of connective tissue; there is a greater abundance of lipid granules in the Sertoli cells; the spermatogenesis is not so active and the spermatozoa are not so numerous. Under an oil-immersion many of the spermatids and spermatozoa seem to be ill-formed and tend to be stained with the acid rather than the basic dye (*vide* Plate I).

In the second stage there is a complete or almost complete arrest of spermatogenesis, but many of the tubules still contain spermatogonia and spermatocytes and even spermatids; the cells of Sertoli contain abundant lipid granules; the basement membrane is greatly thickened and there is excess of interstitial tissue.

In the third stage the tubules are very small; there is a complete or almost complete disappearance of the spermatogenic cells, the only cells remaining being the Sertoli cells, which may or may not contain coarse lipid granules and droplets. The interstitial tissue is often dense and always increased; it contains a variable amount of lipid.

The most interesting stage is the first, and Dr. Such and I are continuing our researches in order to see if it is possible to determine the earliest phase of this progressive decay of the germ-cells in the formation of the spermatozoa in the spermatids. So far as I am aware no account exists of the normal process in the human subject. We shall look for changes in the centrosome, in the mitochondria and in the archiplasm that forms the head of the spermatozoon. But the difficulties, as you may imagine, are great to detect pathological changes in bodies lying in the spermatids, which themselves are no larger than a red blood-corpuscle; moreover, the spermatids exist in unlimited numbers. Yet in respect to the testis this is a fundamental proposition which requires answering in order to prove how it comes to pass that there is a primary failure in the specific energy of the nuclear substance of the male germ-cell. The fact that the Sertoli syncytial or nurse-cells contain abundance of lipid in testes where there is a failure of spermatogenesis indicates that this failure is not due to a lack of the raw material, but that the spermatogenic cells are unable to utilise this phosphorised lipid ester by exhibiting evidence of a formative capacity to build up fresh nuclear substance.

The Pathological Changes in the Ovaries in Dementia Præcox.

In the ovary, where the primitive follicles are in limited numbers, the condition of the germinal vesicle and germinal spot (nucleus and

nucleolus) in respect to the chromosomes and chromatin network can be studied comparatively in the normal and in dementia præcox much more easily than in the testes.

Our preliminary investigations show that in dementia præcox the nucleus of the ovum in the primordial follicles is deficient in the chromatin network ; the nucleus is swollen, often irregular in outline, and the intranuclear network thin and sometimes ruptured, giving the nucleus the appearance of being vacuolated. Not infrequently the nucleolus takes the acid dye more than the basic. The changes are like those seen in the nucleus of the cortical neuron. Not infrequently frozen sections stained with Scharlach and the silver method show fatty degeneration changes of the germinal vesicle. The fatty degeneration of the nucleus of the primordial follicles can be seen even under a low-power magnification. Occasionally a follicle can be seen with its single layer of granule-cells separated from the theca interna, indicative of degeneration of the ovum. When these follicles are examined with an oil-immersion lens it is seen that the ovum is dead or dying, for it does not show the intra-nuclear network ; only the nucleolus is visible, and the remainder of the nucleus consists for the most part of intra-nuclear, coarse and fine lipoid granules. I have placed under the microscope sections to illustrate this degenerative change, which is striking when a comparison is made with the appearances presented by the ova contained in the ovary of a young woman who committed suicide (*vide* Plate VIII, fig. 1).

Another interesting fact revealed by this method of staining is, that in the normal ovary around the primitive follicles are abundant fine lipoid granules similar to those seen in the Sertoli cells. These same granules can be observed in similarly stained sections of the pituitary gland and between the cubical cells lining the colloid vesicles of the thyroid ; they are probably oxidase granules. In several cases of dementia præcox frozen sections of the ovaries stained in a similar manner we have not found these granules, or, at any rate, far less abundant in the stroma around the primordial follicles. Therefore these preliminary investigations tend to show in the ovary (*vide* Plates VIII and IX) :

(1) A failure of the primordial follicles to mature, even to the extent of a single layer of cells, except rarely, and then not to go beyond a single layer of cells to form a zona granulosa, which is generally separated from the theca interna.

(2) A degeneration of the nucleus.

(3) Replacement by ingrowth of stroma.

There is, I think, then, considerable pathological evidence forthcoming to show that dementia præcox is the result of an inborn germinal deficiency of productive energy of the reproductive organs

associated with a progressive deterioration of psycho-physical energy, the morbid manifestations of which show themselves in the whole body, but especially in the brain, particularly and firstly in its highest evolution level.

CONCLUDING REMARKS.

In conclusion I wish that I had the philosophic understanding and the command of language to express my thoughts as eloquently and lucidly as Dr. Maudsley possessed.

During fifty years his great mind was reflected in numerous classical works, now too little read and appreciated. His essays on Hamlet, Swedenborg and Vital Energy are remarkable efforts of his earliest philosophic literary attainments. I am showing here to-day the MS. of some of his works, and it will be observed how very few are the corrections in his recent great book on *Organic to Human*—a remarkable proof of the logical sequence of thought he possessed, combined with a remarkably full and accurate memory. His classical work *The Physiology and Pathology of Mind* was subsequently published in separate parts as *The Physiology of Mind* and *The Pathology of Mind*. An eminent American psychiatrist, now dead, told me that Prof. James of Harvard recommended his students to read these two books, and I can assure members of this Association who are not familiar with these works, they will derive, as I have done, much profit from reading and studying them.

I had the privilege of knowing Dr. Maudsley personally for the last ten years of his life. I had many opportunities of conversing with him on most subjects. I was always struck by his remarkable insight into the characters and conditions of men; he did not suffer fools gladly, not even clever fools, and he had an especial contempt for all that was shallow and superficial. His thoughts, like his writings, were tinged with pessimism and the vanity of things human. Hid beneath a hypercritical and often cynical exterior was a very kind and affectionate nature, which was readily touched by the real suffering of others.

Maudsley received no titular honour. Nevertheless it was recognised by those who knew, and it is that which matters, that he belonged to an "order of merit" that will not perish and be forgotten. His contributions to medical science and philosophy and the foundation of this hospital will, aided by this lectureship, keep his memory ever green. It can be truly said of Henry Maudsley—

"Exegi monumenta aere perennius."

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Idem.—"Studies in the Pathology of Dementia Præcox," *Proc. Roy. Soc. Med.*, vol. xiii, 1920 (Section of Psychiatry), pp. 25-63.

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The reader is referred for Plate I to the article on the
"Normal and Morbid Conditions of the Testes from Birth to
Old Age in One Hundred Asylum and Hospital Cases."

The reader is referred for Plates VI, VII, X and XI to the
article on the "Studies in the Pathology of Dementia Præcox."



FIG. 1.

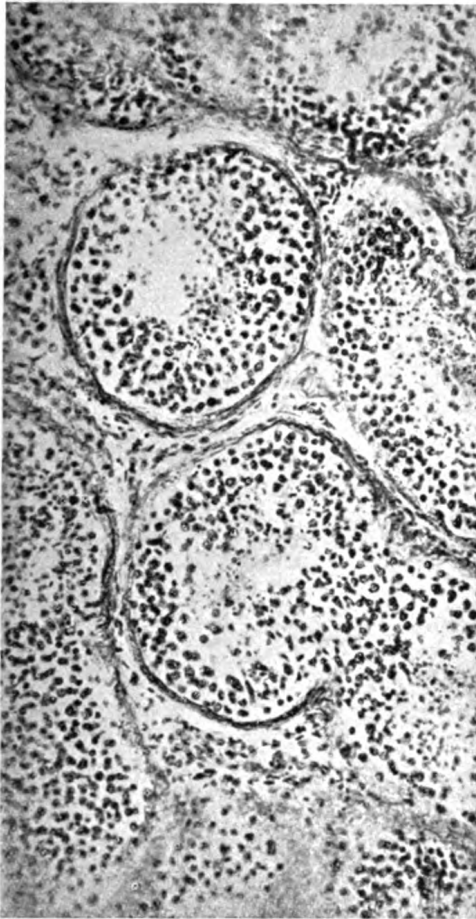


FIG. 2.

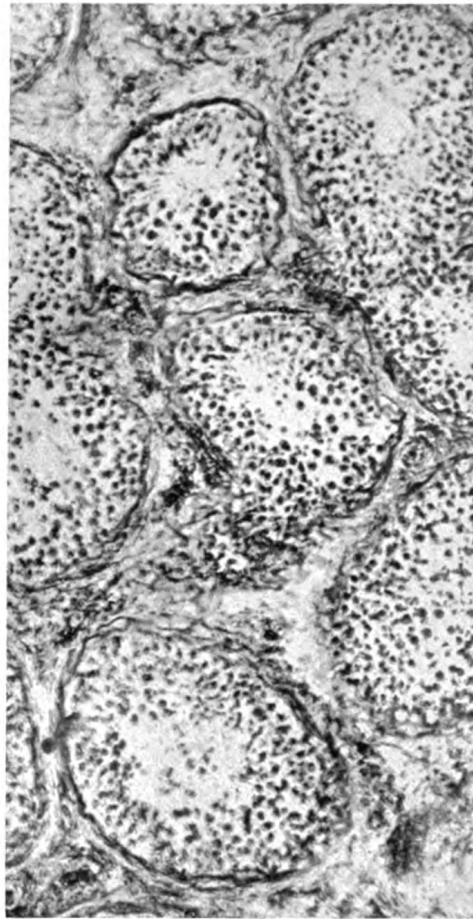


FIG. 1.—Section of normal testicle of youth æt. 21, who died of infective endocarditis. Shows the normal testis with active spermatogenesis.

FIG. 2.—Section of testis of F. A. E—, æt. 26. Dementia præcox. Mental symptoms twenty-two months. Death from dysentery. Testes weighed each 19 grm.; normal naked-eye appearance. Shows the very earliest stage with some evidence of interstitial tissue and diminution of spermatogenesis.

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FIG. 3.

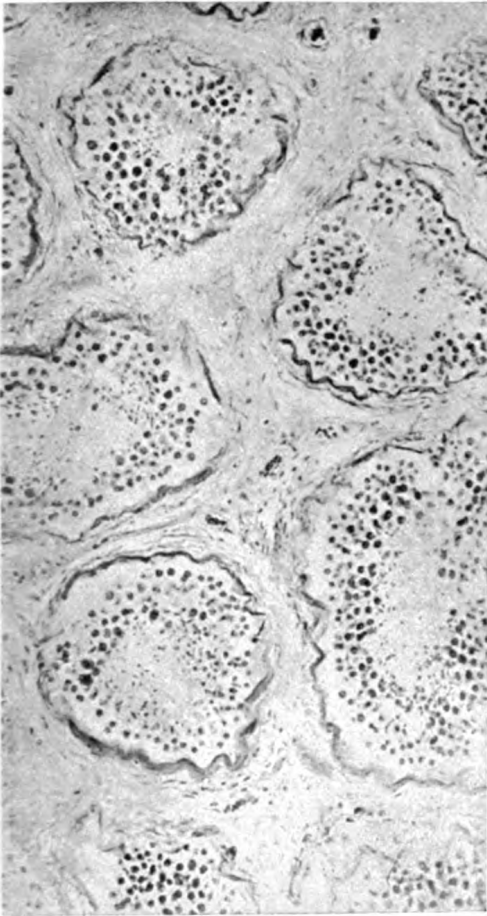


FIG. 4.

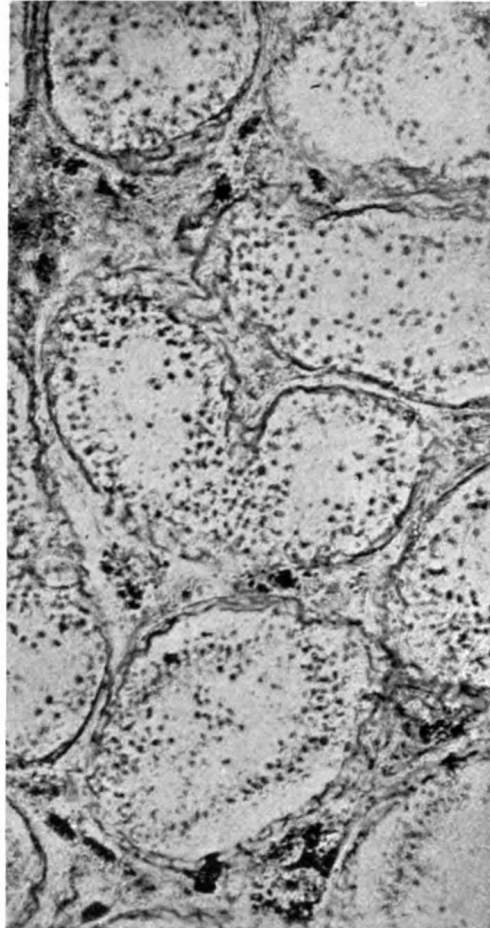


FIG. 3.—Section of testis of E. T—, æt. 19. Twenty-three months' duration of mental symptoms. Testes 19 and 16 grm. each. Abundant spermatozoa in vesiculæ seminales, many degenerated. Exhibits a later stage of regressive atrophy in which spermatogenesis is still active, but there is a deficiency of spermatogenic cells, increase of interstitial tissue, with shrinking of the tubules and thickening and crinkling of the basement-membrane.

FIG. 4.—Section of testis of W. H—. Soldier discharged after two years three months' service; then delinquencies of various kinds. Admitted to Long Grove Asylum, June, 1918, æt. 20. Death from lobar pneumonia seventeen months after admission. Testes—weight, 13·8 grm. right; 15·8 left. Arrest of spermatogenesis with shrinking of the tubules, thickening and crinkling of the basement membrane.

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FIG. 5.

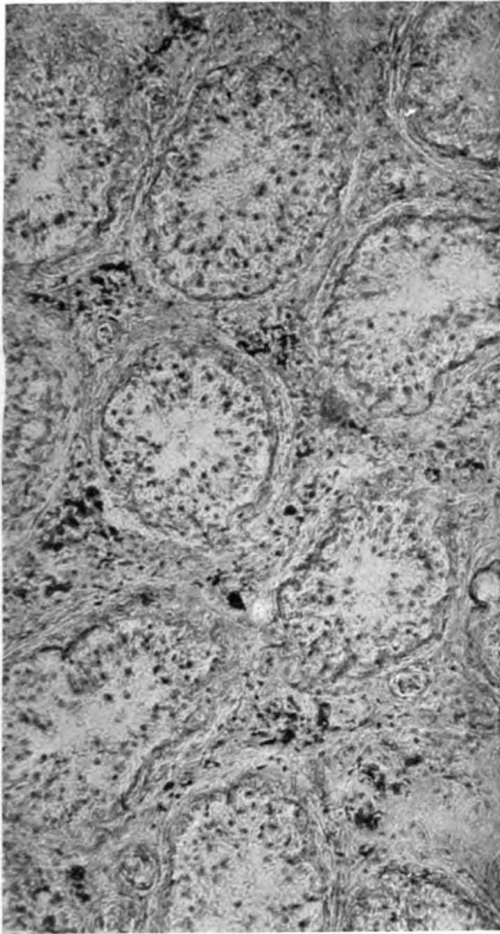


FIG. 6.

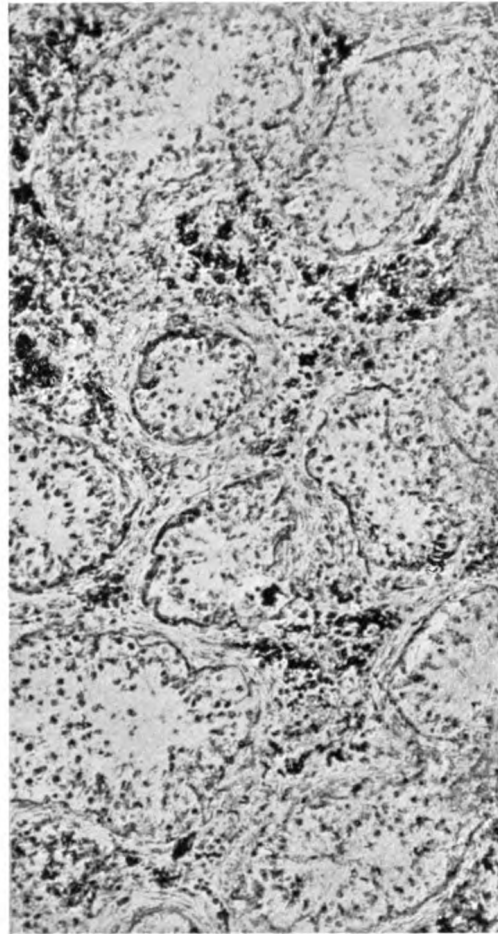


FIG. 5.—J. S. C—: age at death, 29; admitted at the age of 24. Testes 10 grm. each. Complete arrest of spermatogenesis, shrinking of the tubules, very marked diminution of spermatogenic cells. Great increase of interstitial tissue, thickening and crinkling of basement-membrane.

FIG. 6.—P. H—, æt. 17 years 6 months onset of mental symptoms. Admitted to asylum at age of 18; died æt. 20 of pulmonary tuberculosis. Testes each 9 grm. Final stage of regressive atrophy: Tubules much shrunken, only contain Sertoli cells with lipoid granules contained in them; marked thickening of basement-membrane and dense fibrosis of interstitial tissue.

Magnification of all these photo-micrographs on Plates II, III and IV is 150. These sections were stained by the special silver method of del Rio Hortego. A full account of this method and of the clinical histories of them and many other cases will be published by Dr. Prado y Such and myself shortly.

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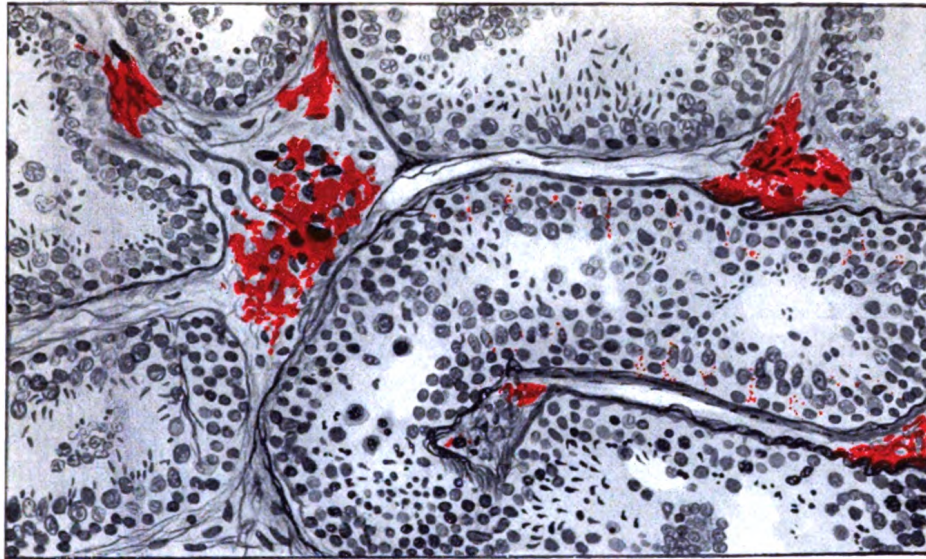


FIG. 1.—Section of normal testis stained by scharlach and del Rio Hortego silver method. Observe the active spermatogenesis and the relatively small amount of lipid granules the Sertoli cells. Abundance of lipid in the interstitial tissue.

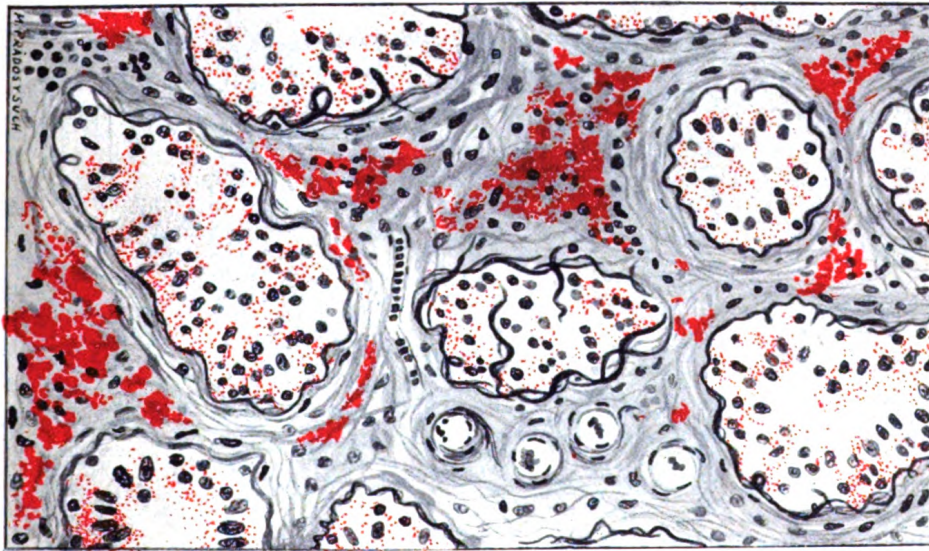


FIG. 2.—Section of testis of J. S. C— (fig. 5, Plate IV). Observe the complete arrest of spermatogenesis, atrophied tubules and increase of interstitial tissue with lipid. The Sertoli cells contain numbers of fine lipid granules.

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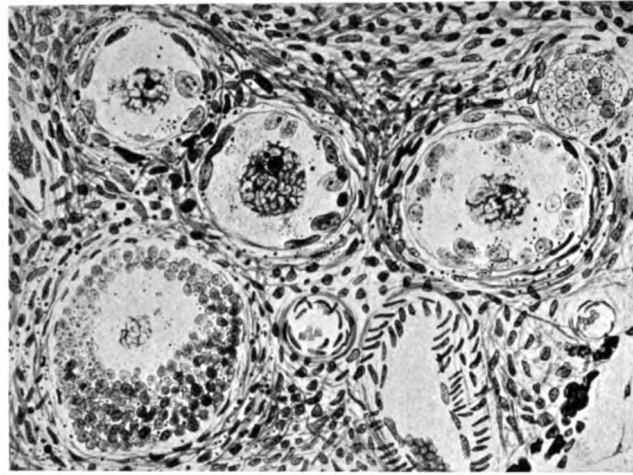


FIG. 1.—Frozen section of ovary of a young woman who committed suicide. Stained by special silver method and scharlach. This shows primordial follicles containing ova with a well-marked chromatin network of the nuclei and surrounding granulosa cells. The largest follicle is not cut through the centre and shows active proliferation of the granulosa cells. The interstitial cells with many nuclei are seen, and scattered about in the tissue are numbers of black (in section red) granules of lipoid—presumably oxidase granules.

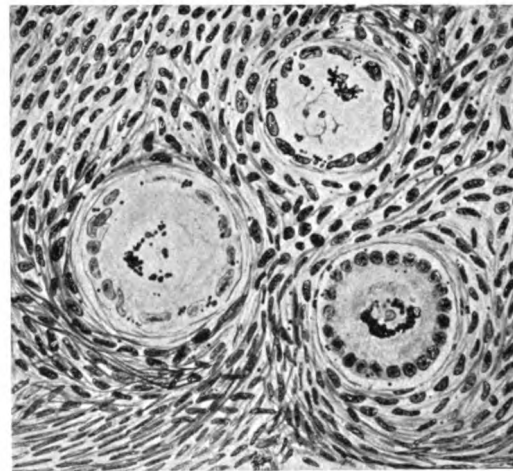
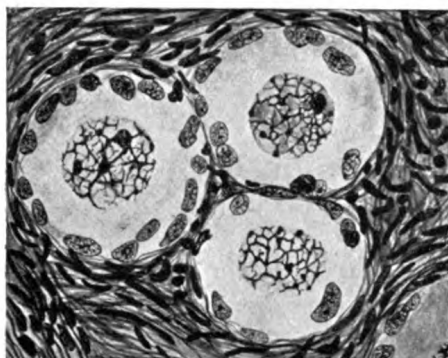


FIG. 2.—Frozen section of ovary from a case of dementia præcox stained by special silver and scharlach method. Observe the absence of chromosomes in the nuclei of the ovary and replacement by droplets and coarse granules of lipoid stained red but appearing black. Comparatively few oxidase lipoid granules are seen in the interstitial tissue.

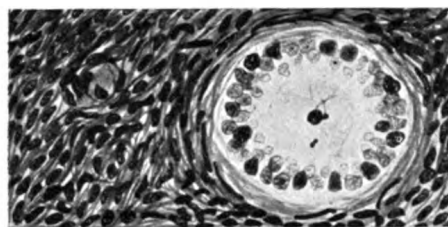
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A.



B.



C.

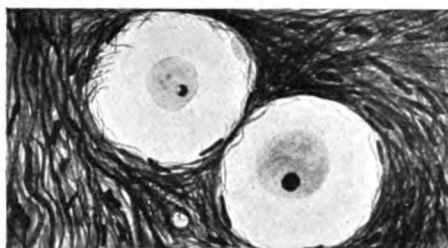


FIG. 3.—Three frozen sections of ovaries stained by silver method to show changes in the primordial follicles.

A. Normal showing three primordial follicles, each showing well-developed chromatin intranuclear network.

B. Primordial follicle from a case of dementia præcox following pregnancy. The nucleus shows nucleolus, but hardly a vestige of intranuclear chromatin. The cells of granulosa layer unequally stained owing to degeneration, enclosed in a theca interna. This follicle is commencing to degenerate owing to a lack of vital energy.

C. Final stage of regressive atrophy of primordial follicles from another case of dementia præcox following pregnancy. The nuclei show no trace of chromatin network, the nucleoli are alone stained; there are no granulosa cells and the interstitial tissue consists of dense fibrous tissue with few nuclei.

Plates VIII and IX are drawings executed by Dr. Prado y Such with an ocular 4 and $\frac{1}{12}$ oil-immersion lens.

To illustrate Maudsley and Morison Lectures by Sir FREDERICK MOTT.

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(Revised reprint from the *British Medical Journal*, November 22nd, 29th and December 6th, 1919.)

Normal and Morbid conditions of the Testes from Birth to Old Age in One Hundred Asylum and Hospital Cases, by Sir Frederick W. Mott, K.B.E., M.D., LL.D., F.R.S., F.R.C.P.

THE material dealt with in this article was collected from 100 cases of deaths, occurring at all ages from birth to 86, in London asylums and various civil and military hospitals.*

In a majority of the asylum cases, especially those dying at Claybury and upon which I made the *post-mortem* examination, the contents of the vesiculæ seminales were examined. In a small number of cases the thyroid, adrenals, and pituitary glands were also examined. In all the hundred cases the testes were weighed and subsequently examined by the histological methods to be described.

MACROSCOPIC APPEARANCES OF THE TESTES AFTER PUBERTY.

It was found that sections of fresh or formol-hardened testes, when examined with a hand lens, revealed naked-eye pathological changes in a majority of the asylum cases; the converse was noticeable in the adult hospital cases.

In the normal testes occurring in cases of death from injury or disease without mental symptoms, the weight of each of the organs, as a rule, was normal. Upon section the tubuli seminiferi appear white, plump, and closely packed together, without appreciable intervening fibrous tissue.

In the asylum cases the most marked deviation from the normal condition was found in two groups of cases—namely, (1) general paralysis, (2) dementia praecox.

(1) The weight of the testes in general paralysis varied considerably. It was not infrequent to find one testis considerably smaller than the other, and the tunica albuginea adherent. The weight is not always an index of the functional efficiency or otherwise. There was no correlation between the naked-eye cortical changes in the brain in general paralysis and the morbid changes in the testes.

In a relatively small proportion of the cases of general paralysis examination with a hand lens of a sectioned testis showed no abnormal naked-eye appearance. In the majority of the cases, however, strands and localized patches of fibrous tissue of variable extent and degree separated the white seminiferous tubules and some other tubules might appear smaller than normal.

* The expense incurred for drawings, illustrations, and aid for this research was assisted materially by a grant from the Board of Control. I also wish to express my obligations to the superintendents, medical officers, and others who have kindly provided me with some of the material for this research.

(2) In the regressive atrophic condition met with in the great majority of cases of dementia praecox the tubules appeared attenuated and less plump than the normal, and were either of a greyish colour or did not present the uniform milky white appearance of the normal tubules. There may or may not be an increase of interstitial tissue. As a general rule, the degree of morbid naked-eye change of the testes in dementia praecox conforms to the duration of the mental disease and the clinical signs and symptoms of the mental decadence rather than to any obvious naked-eye changes or defects in the brain. In general paralysis the dementia corresponds in great measure to the degree of cortical destruction; nevertheless, there is no correlation in this disease between the brain atrophy and the testicular atrophy.

With the exception of cases of senile dementia and congenital imbecility with epilepsy, the testes in other cases dying in the asylum did not, as a rule, show any marked departure from the normal—for example, cases of epileptic insanity, Korsakoff psychosis, paranoia, and manic depressive insanity.

Table of Classification of the One Hundred Cases from which the Material for Investigation was Obtained.

<i>Asylum Cases.</i>				<i>Hospital Cases.</i>			
1. Dementia praecox	23	1. Born dead or dying before puberty	8
2. General paralysis	23	2. Dying after puberty of various diseases	8
3. Juvenile general paralysis	4	3. Under puberty death from injury shock	1
4. Psychoses—for example, manic depressive insanity, paranoia....	7	4. Over puberty death from injury shock	1
5. Epilepsy	3	5. Military cases—injury of brain or spinal cord, with sepsis of variable duration	8
6. Congenital epilepsy, with idiocy or imbecility	4				
7. Organic brain disease	5				
8. Imbecility	2				
9. Senile dementia (octogenarians)	3				
			74				26

HISTOLOGY.

The following methods of histological investigation were employed :

HISTOLOGICAL METHODS.

1. Examination of the contents of the vesiculae seminales by dark-ground illumination and an oil-immersion lens.

2. An emulsion of the testis was prepared by rubbing up a small portion of the organ in a mortar with Ringer's fluid. The emulsion was examined with an oil-immersion lens and dark-ground illumination. The same method was employed in examining the brain for spirochaetes.

3. Smears of the seminal contents of the vesiculae were stained by Delafield's haematoxylin and eosin, by Heidenhain's haematoxylin and eosin, and with Giemsa or polychrome-aniline dye stains.

4. The organs were hardened in 10 per cent. formol solution, and portions of them were cut into sections with the freezing microtome. These sections were stained with scarlet* or Sudan III and some were counterstained with haematoxylin; subsequently the sections were mounted in Farrant's solution. This method was employed to demonstrate the amount and distribution of the lipid substance. In some cases the sections were placed in Marchi fluid.

5. Portions of the gland were cut out into sections of uniform thickness, after embedding in paraffin or treating with the celloidin method. Some pieces were stained in bulk with haematoxylin and eosin, treated first by celloidin method, and after placing in chloroform subsequently embedded in paraffin. This method is very useful, as thin serial sections can be obtained without any shrinking of the tissue. Giemsa, polychrome or the Heidenhain, eosin and van Gieson stains were used for staining the sections. The films and sections were mounted in neutral Canada balsam.

THE DEVELOPMENT OF THE TESTES FROM BIRTH TO PUBERTY.

The development under normal conditions, and under abnormal and diseased conditions, other than congenital syphilis, will now be considered.

At Birth, and in Infancy and Early Childhood.

1. The testes of full term identical twins, born dead but in a healthy bodily condition, also of a healthy full term child, born dead, were examined.

The histological appearances of sections were as follows :

The seminiferous tubes, seen in longitudinal, oblique, and transverse section, are filled with embryonic cells, lying upon a thin membrana propria; there is no sign of differentiation. The cells have round or oval nuclei, with a delicate reticulum of chromatin and a dense membrane. The cells with round nuclei are the spermatogonia; those with oval nuclei are the cells of Sertoli. The amount of cytoplasm is relatively small, it is faintly stained with eosin and presents a homogeneous appearance. The interstitial tissue is relatively more abundant than the tubules at this stage; it is like ordinary connective tissue, except that *there are groups of fairly large polygonal epithelioid cells scattered through the organ—the cells of Leydig; these cells may be seen occasionally in double rows, with an interval between like a tubular gland (Fig. I). These special interstitial cells are very numerous in all the sections. The cytoplasm is three times as abundant as the nucleus; it is stained deeply by eosin. A lipochrome substance may be observed in many of the cells, exactly like the lutein found in the cells of the ovary, in the form of fine light-yellow granules, distributed throughout the cytoplasm. These cells are not unlike liver cells; they stain red with scarlet (see Fig. I).*

2. Sections of a testis of a child, aged 4 months, dead of pneumonia, with a syphilitic rash on the legs, back and head, showed the following appearances :

*Scharlach.

The seminiferous tubes have developed considerably by a proliferation of the embryonic cells, so that they appear nearly double the size of the tubes at birth ; the interstitial tissue appears relatively less (Fig. II). A few fine lipoid granules, stained yellowish-orange, are seen scattered in the seminiferous tubules, and abundant scarlet-stained granules are seen in the interstitial tissue. *Only a few interstitial cells are now seen ; they are smaller than in the testis of the infant at birth.* They can, however, be recognized by the clear outline of the cell—the round, comparatively deeply-stained basophil nucleus, which is easily discerned in the eosin-stained cytoplasm. The lipochrome in the interstitial cells is less obvious than at birth. The appearance of lipoid granules in the seminiferous tubules and in the interstitial tissue may be explained by supposing that it has been, and is still being, utilized by the embryonic sperm cells in their formative activity and proliferation ; the interstitial cells now disappear or assume a resting stage, in which they will remain until puberty, when they again appear and become active in the spermatogenic function for reproduction (Fig. V).

3. The testis of a child aged $3\frac{1}{2}$, dead of broncho-pneumonia (Fig. III), exhibits smaller tubules than in Fig. II ; there is more interstitial tissue, and these two facts suggest that there is some arrest of development.

It is possible that when the interstitial cells of the infant are no longer active the internal secretion has already performed its office of impressing on the body the male characters and upon the nervous system the special instincts and affective characters of the male sex. We do not find any evidence of maturation of the male germ cell ; it is otherwise in the female, for sections of the ovary of a female infant aged 18 months showed complete Graafian follicles, with a perfect ovum, zona pellucida, discus proligerus and zona granulosa. It is a reasonable hypothesis to suppose that the cells of the zona granulosa and discus proligerus of these Graafian follicles of the infant produce an internal secretion which impresses on the central nervous system the instincts of the female and the psychic characters peculiar to the sex. Moreover, the continual formation of follicles which do not undergo dehiscence till menstruation occurs may, through a bio-chemical influence on the somatic cells, impress female characters, not only on the mind, but on the growth of the body. If the male characters are dominant in the somatic cells this internal secretion would play an important part in determining the female characters.

EARLY STAGE OF ACTIVITY OF THE GLAND.

4. The testes of a boy aged 9, who died of shock from injury, exhibited appearances very similar to the following though less advanced.

5. The testes of a boy aged 11, who died of fracture of the base of the skull, were examined, with the following results :

The basement membrane of the tubules is more distinctly seen ; the tubes are larger generally speaking filled still with only cells such as are seen in the infant, but here and there are observable early stages of formative activity recognizable by karyokinetic figures in the nuclei of some of the spermatogonia and spermatocytes ; the sustentacular cells of Sertoli may now occasionally be clearly differentiated, but these syncytial cells contain but few lipoid granules (Fig. IV). There is no evidence of spermatids. *There is some slight fine granule lipoid staining in the tubules, but no interstitial lipoid, so that the interstitial cells are still practically in the resting stage, appearing as flattened nucleated cells or round nucleated cells, with a small amount of cytoplasm, which when examined with an oil immersion is seen to be stained faintly pink.*

AFTER PUBERTY.

Adolescent.

The vesiculæ seminales and testes of a healthy boy aged 15 (Case 6), who died twenty-four hours after a motor accident which crushed the chest, showed the following histological appearances :

Seminal Fluid.—The spermatozoa, observed by dark-ground illumination and in stained films, of the semen from the vesiculæ seminales are not so numerous, and appear to be smaller than those in the semen of the normal adult. Spermatozoa were found also in an emulsion of the testis, but they did not appear to be as large as those found in the emulsion of the testis of the adult.

Sections of the Testis.—The tubules are now fully developed, closely approximated, and twice the diameter of those seen in the boy of 11. Nearly all the tubes now show abundance of spermatozoa, and active spermatogenesis in all stages (Fig V). Numerous groups of interstitial cells are seen, and coarse granules of scarlet-stained lipoid within and around these cells are observable. The interstitial cells appear to lie outside the lymph space surrounding the basement membrane of the seminiferous tubes. *The fine orange-stained granules of lipoid within the sustentacular cells are not nearly so abundant as in corresponding cells of the testis in the adult.* (Compare Figs. VI and VIII.)

It is obvious, therefore, that with the dawn and development of the sexual desire there occur two histological changes—namely, the reappearance of the interstitial cells in an active state, and the accumulation in and around them of these orange-stained granules ; and this may be regarded as an indication of the presence of a phosphorized lipoid, which may serve as the raw material from which can be built up the nuclein necessary for the active formative cell processes connected with spermatogenesis. I have purposely said may because the other view is that the nucleic acid is formed from protein and circulating inorganic phosphates (see below), but physiological chemistry has not yet settled the synthetic processes underlying the formation of nucleic

acid, which is the main chemical substance in the constitution of the head of the spermatozoon. A further discussion of this subject will appear in another monograph when the results of chemical analysis of the testes in health and disease which are now being undertaken are completed.

Adult.

The following cases afforded an opportunity of examining the testes in healthy adults.

CASE 7.

W. L., an engine driver, fell off his engine and was killed. He was brought into Charing Cross Hospital. Sections of the testes showed normal spermatogenesis in all stages; the number of the spermatozoa in the tubules was not so great as in most normal cases. The interstitial cells of Leydig were extraordinarily well seen forming large groups in the loose connective tissue between the tubules (Fig. VII). The basement membrane of the tubules was not thickened. Frozen sections stained with scarlet dye and haematoxylin showed most clearly the cells of Leydig filled with the orange-stained granules of lipoid. The cells of Sertoli are likewise filled with these fine orange-stained granules.

Among the cases dying of injury and in which spermatogenesis is normal, it is remarkable how variable is the readiness with which the cells of Leydig can be discerned. In some, as W. L., they are seen in every low power field in every section; in others they can only be found by searching.

Among asylum cases it has struck me that the testes of general paralytics show these cells in greater numbers than the testes of other forms of insanity. Too much importance must not, however, be attached to this statement, for unless serial sections of both testes were made and examined, a definite conclusion that the hormone cells were in greater numbers in the testes of persons suffering with general paralysis than other persons dying in the asylums is unwarranted.

CASE 8.—*Normal Spermatogenesis in the Adult.*

F. H. C., aged 24, was admitted to Charing Cross Hospital suffering with multiple injuries of the pelvis, and died the same day from shock.

Sections of the testis from this case stained for lipoid showed abundant granules in the syncytial cells—so abundant as to form a ring around the tubule within the basement membrane (Fig. VIII). Comparatively little lipoid was seen in the interstitial tissue. Frozen sections stained with haematoxylin and scarlet and mounted in Farrant solution showed interstitial cells containing lipoid granules, but there was considerable congestive stasis in the blood vessels and capillary haemorrhage (doubtless the result of the injury), and this would account for the relatively small amount of lipoid in the interstitial tissue. The tubules show active spermatogenesis in all stages (Fig. IX). This case will therefore serve for the description of normal spermatogenesis.

NORMAL SPERMATOGENESIS IN THE ADULT.

A section of the normal seminiferous tubule shows a well defined *membrana propria*, with flattened nuclei, supporting several layers of cells. The layer of cells lying on the basement membrane consists of spermatogonia, and between the spermatogonia are the syncytial cells of Sertoli, which are larger, have oval nuclei, and project inwards between the various layers of cells which are undergoing successive stages of active mitosis, incidental to spermatogenesis. The cells of Sertoli, or sustentacular cells, are particularly rich in lipoid granules. Within the above mentioned outer layer of cells are larger cells (the spermatocytes), the large nuclei of which show all forms of karyokinesis. The spermatocytes are products of division of the spermatogonia, each of which, on dividing into two, gives rise to one cell like itself, and another which grows larger, and passes into the second layer to form a spermatocyte.

The spermatocytes undergo a division. A product of the division of the spermatocyte again divides, giving rise to spermatids, the number of chromosomes becoming reduced to half the number during this process. The spermatids are small cells with spherical nuclei; they elongate, and the nucleus becomes shifted to one end. The young spermatozoa thus formed collect into irregular groups, and appear deep in the sustentacular cells of Sertoli, which serve as a support and source of nourishment to the young spermatozoa. As they grow and acquire their tails at this stage of spermatogenesis the heads appear to be nearer the lumen of the tubule, and the tails of the spermatozoa project freely into the lumen of the tubule; a little later in the process of development the spermatozoa grow in size and are pushed further towards the lumen, and eventually become completely liberated (Fig. IX).

Examination of the spermatids in haematoxylin eosin stained sections with an oil immersion shows a nucleus stained deeply with the basic dye surrounded by a thin layer of eosin stained cytoplasm. These develop into spermatozoa in the following way: The nucleus becomes shifted to one end, and assumes an oval and then a lance-head shape, and behind this is seen the eosin stained cytoplasm which later, in the Sertoli cells, grows to form the main part of the tail.

The process is continually going on in the seminiferous tubules of the testis, successive crops of spermatozoa being continually produced. The various stages of development may be observed in the normal testis, or even within the limits of a single tubule (Fig. X).

The reduction in the number of chromosomes, which takes place in the formation of the spermatids, is analogous to the casting out of the polar bodies of the ovum; both processes constituting a preparation for the conjugation of the male and female gamete which takes place in the fertilized ovum.

THE LIVING SPERMATOOZON.

The spermatozoon is a living organism produced in incalculable numbers by the testis during the greater part of a healthy man's life, and it may be regarded as the most remarkable organism in Nature, for concealed in its minute structure and bio-chemical organization is the specific energy of the highest vital dynamics of evolution. In a normal emission of man, Lode calculated that there are about 226,000,000 spermatozoa, and that 339,385,500,000 must be produced in man between the ages of 25 and 55.

The semen is the mechanical medium in which the spermatozoa move, and when ejected it is mixed with the secretion of the prostate and Cowper's glands.

Examination of the Contents of the Vesiculæ Seminales Post Mortem.

The seminal secretion of the testes is stored in the vesiculæ seminales. There may be a biological advantage in this, for I have found that examination of the semen in the vesiculæ seminales of people dying of various diseases show spermatozoa in various stages of degeneration. Moreover, in two of the cases the contents of the vesiculæ examined by dark-ground illumination showed that some of the spermatozoa were still alive and active eight hours after the patient's death. Now the specific energy of these active spermatozoa must have been greater than the inactive dead organisms. Consequently, in a person suffering with disease it is probable that only those with a normal specific energy survives; thus only the fittest are left for fertilization. As will be shown, there is reason to believe that this degenerative process of the spermatozoa may commence in the early stages of normal spermatogenesis.

In many cases of disease, especially dementia praecox, the appearances of the spermatozoa proved that for some time past no living spermatozoa had existed; they all showed appearances of marked degeneration (Fig. XI), the staining reaction was not normal, the heads showed obvious bio-chemical and morphological changes; the tails were broken off from many; the heads gave an oxychromatin reaction, staining with the eosin instead of the haematoxylin. Many showed only fine granules of chromatin stained by the basic dye.

I have placed seminal fluid from the vesiculæ in a sterilized sealed-up tube and kept it for more than four months, and the same forms could be seen as were observed in the films made at the time the seminal fluid was first collected. This fact is of importance, for it shows that spermatozoa may be found in the vesiculæ when active spermatogenesis has for a long time ceased.

SUMMARY OF NOTES OF SPECIAL CASES OF INTEREST.

In the vesiculæ seminales of a demented man, aged 81, who died of pneumonia, abundant spermatozoa were found; some in various stages of degenera-

tion, but quite a number of the heads took the basic dye as if they were still capable of fertilization. Examination of sections of the testes showed that the majority of the tubules exhibited all stages of active spermatogenesis.

In a case of juvenile general paralysis of the insane, fluid from the vesiculæ seminales, examined by dark-ground illumination in pericardial fluid, was found crowded with spermatozoa, a few very active. The majority stained normally with the basic dye.

In a case of typical dementia paralytica, aged 69 at death, in which there was advanced brain degeneration, arterio-sclerosis and cirrhosis of liver, death occurring from bronchopneumonia, the fluid from the vesiculæ showed abundance of spermatozoa, mostly degenerated. Still, active spermatogenesis must have been going on while he was in a state of profound dementia.

In another case of paralytic dementia the patient was in good general health till he had seizures which continued for a fortnight when he died of exhaustion. My notes state that there is little active spermatogenesis in the testes. It is probable that since the patient began to have seizures with prolonged asphyxial conditions spermatogenesis had been arrested. Prolonged venosity of the blood may have interfered with the oxidation process necessary for biochemical decomposition and recombination processes of nuclear formation. It may be concluded that the vesiculæ seminales, which were filled with spermatozoa, had them stored there before he had the seizures, and, as the patient was in an unconscious or semi-conscious state the whole time, they were never evacuated.

THE SEMINAL FLUID IN DISEASE.

THE EXAMINATION OF THE FLUID IN THE VESICULÆ SEMINALES OF CASES OF GENERAL PARALYSIS OF THE INSANE.

Among twelve successive cases of general paralysis of the insane, of all ages and in all stages of the disease, as regards cortical decay and destruction, spermatozoa were found in the vesiculæ seminales of eleven, and in such a condition as to support the view that they had, just prior to or not long before death, been possessed of vitality, and were capable of fertilizing. The one case in which no spermatozoa were found in the vesicula seminalis might have shown spermatozoa in the other vesicula had it been examined.

The evidence of recent spermatogenesis afforded by examination of the contents of the vesiculæ in these 12 cases of general paralysis of the insane, accords with the evidence afforded by histological examination of a much larger number of testes, including these 12 and other cases; for I did not find one young or old (excepting a case of juvenile general paralysis of the insane, which began at 8 years of age) in which there was not evidence of active sperma-

togenesis in some of the seminiferous tubules, although usually scattered through the organ was partial or complete destruction of the sperm cells of some of the tubes, leaving only the basement membrane and sustentacular framework (Fig. XV).

Now, one of the common characteristics of general paralysis of the insane is excessive sexual desire, and masturbation is frequent in both the early and demented stage. Yet, although this is so frequent and may extend over years, it has not been sufficient in any one of the large number of cases I have examined completely to arrest spermatogenesis or produce a similar regressive atrophy of the seminal tubules to that met with in the great majority of cases of dementia praecox.

EXAMINATION OF THE SEMINAL FLUID OF THE VESICULAE SEMINALES IN OTHER DISEASES.

Severe head injuries, even with sepsis, do not, as a rule, arrest spermatogenesis. In one case there was a complete arrest. In two cases of bullet-wounds of spinal cord with bedsores and prolonged sepsis there was complete arrest and an appearance of coagulation necrosis of the cytoplasm of the spermatogenic cells (Fig. XIII). Advanced chronic pulmonary tuberculosis of the most extensive nature may not arrest spermatogenesis. This is of importance, because a large proportion of the asylum cases, including especially dementia praecox, die of tuberculosis. Fourteen out of sixteen successive cases of this disease died of pulmonary tuberculosis.

MASTURBATION DOES NOT CAUSE ARREST OF SPERMATOGENESIS.

A case of mania was of interest in showing that the vesiculae seminales may be crowded with spermatozoa and the testes show normal spermatogenesis, although the notes state that the patient during twenty-five years in the asylum was a pronounced masturbator. It cannot be therefore asserted that masturbation *per se*, even when continued over a great number of years, can produce regressive atrophy of the testes and arrest of spermatogenesis in a male attacked by insanity in adolescence.

CANCER AND SPERMATOGENESIS.

A patient, J. G., aged 67, suffered with dementia and died of carcinoma of the stomach. The testes weighed respectively 17 and 15 grams. There was complete arrest of spermatogenesis, but the vesiculae were crowded with spermatozoa, most of them degenerated. This seems to show that the active cell formation of a rapidly growing carcinoma of the stomach may, by its devitalizing action and utilization of all the materials circulating in the blood for nuclear formation, arrest spermatogenesis.

Another case of chronic alcoholic neuritis, aged 65, with Korsakoff psychosis, cirrhosis of the liver and ascites, was of special interest, for the vesiculæ seminales contained abundance of spermatozoa, but the testes showed a complete arrest of spermatogenesis. It may be assumed that the spermatozoa found in the vesiculæ were formed during the morbid condition above mentioned. But an active carcinomatosis had taken place in the liver, and it is possible to associate the arrest of spermatogenesis, as in the former case, with the active nuclear formation in the liver. This, however, is merely conjecture; it may be only a coincidence, but it is a suggestive coincidence that makes it desirable to pursue the matter further by an examination of the testes in a number of cases of death from new growths.

EXCESSIVE SUPPURATION AND SPERMATOGENESIS.

A case of very extensive suppurative pericarditis of some weeks' duration showed arrest of spermatogenesis in the testes, although the vesiculæ contained abundant spermatozoa, probably formed before the suppurative process occurred. Here, again, an enormous nuclear proliferation and destruction of nuclear matter must have occurred.

NO ARREST OF SPERMATOGENESIS IN CHRONIC MICROBIAL INFECTIONS.

In cerebro-spinal meningitis, in manic depressive insanity, epilepsy, melancholia, and cases of other forms of insanity dying in the asylum spermatogenesis was still active in spite of fatal microbial disease—for example, acute and chronic tuberculosis and dysentery, which are very common causes of death in asylum patients. Again, bronchopneumonia due to inhalation of food (sometimes with gangrene of the lung), influenza and typhoid fever are frequent causes of death of the insane.

In hospital cases the same applies. This leads one to ask whether the important genetic function is protected from the effects of circulating toxins. The hypothesis I put forward is that the abundant lipoids, consisting of lecithin, cholesterin, and fatty acids, around and in these seminiferous tubules, serve as a protective barrier against toxins.

BULLET WOUND OF SPINAL CORD WITH SEPSIS.

J. Mc.K., age 19, was admitted to Charing Cross Hospital from France, April 22nd, 1915, died April 29th, 1915. The wound was said to have occurred ten days prior to admission. Wound foul and septic in mid-dorsal region, paraplegia complete, cystitis retention overflow. In this case there was a complete absence of spermatogenesis and coagulation necrosis of the spermatic cells, doubtless due to the combined effects of sepsis and the severe lesion of the spinal cord (Fig. XIII).

SPERMATOGENESIS AND OLD AGE.

Arrest of spermatogenesis due to senility occurs at varying ages in different individuals. The organs of three octogenarians suffering with senile dementia who died at Claybury Asylum were investigated, with the following results. Normal spermatogenesis may occur in a very old man, as the following case shows :

CASE 1.—*Senile Dementia.*

W., aged 81, died of pneumonia, February 22nd, 1916. The organs other than the lungs were fairly healthy considering the age. Testicles each weighed 18 grams, and presented a normal naked-eye appearance; an emulsion of the organ revealed, by dark-ground illumination, spermatozoa.

Spermatozoa.—The vesiculæ seminales contained abundance of spermatozoa, many taking the eosin stain only, but a large number showed normal basophil staining spermatozoa. Sections of the organs after hardening in formalin showed, when examined with hand lens, very little excess of interstitial tissue, the seminiferous tubes appeared full, plump, normal in size, and glistening white. Microscopic examination of sections stained by the two usual methods showed normal spermatogenesis in all stages; the basement membrane was not markedly thickened; the interstitial tissue was not increased; the tubules were closely approximated and not atrophied. The cells of Sertoli were filled with orange-stained granules. The interstitial cells of Leydig were present and contained lipid.

In this case the testis was, in fact, as normal histologically as the testis of a much younger man. Indeed, the appearances of virility are in advance of many cases of dementia praecox of the earlier stages, and of many other cases dying in the asylums. In contrast with this are the two following cases :

CASE 2.—*Senile Dementia.*

C., aged 85. Wasserman reaction negative in blood and fluid. Testes not weighed. Vesiculæ seminales not examined. Scarlet preparations. Coarse lipid in the centre of the tubuli seminiferi. Tubules atrophied, interstitial lipid occasionally seen. Hematoxylin and scarlet: no spermatozoa observed anywhere. The seminiferous tubes were in all stages of degenerative atrophy, from an appearance of thick basement membrane, with a few layers of nucleated cells and coarse granules of lipid, to a condition in which the whole tubule was filled with large vacuolated cells; the only part which took the stain was the nucleus, which was flattened against the wall as in a fat cell. These filled the whole lumen, and were apparently the swollen sustentacular cells, filling the space previously occupied by the spermatogonia and spermatocytes. Here and there groups of interstitial cells containing lipid could be seen; they appeared to be undergoing atrophy. In other places they stood out clearly in groups between the markedly degenerated and atrophied tubules.

CASE 3.—*Senile Dementia, Pleurisy with Effusion, fairly Recent.*

T. S., aged 86. Testes: right 11.5 grams; left (small) 8.5 grams. Sections of the testicles showed microscopic appearances in some ways similar to those of the late stages of dementia praecox, except that the membrane propria was not much thickened, the

interstitial tissue was less increased and the epithelium in the tubules showed more nuclear staining. There was a continuous layer of spermatogonia; the cells of Sertoli were not conspicuous. The layer of spermatocytes showed, as a rule, well stained karyokinetic figures of the nuclei but the cytoplasm was vacuolated. This vacuolation was due to lipid contents. Only very occasionally was a tubule found in which there was evidence of heterotypical nuclear division, reduction of nuclear substance, and formation of the spermatids. When spermatids were seen they took the basic dye well. In a few tubules occasional well shaped spermatozoa could be seen. Fairly numerous groups of interstitial cells, smaller than normal, and the majority containing lipochrome pigment, were observable.

Possibly the persistence of the interstitial cells may account for an increased and perverted sexual appetite in old men, due to a stimulation of the desire without the power to perform the sexual act.

ARREST OF SPERMATOGENESIS FROM BIRTH TO ADOLESCENCE.

1. *Complete Arrest before Puberty.*

Examination of the testis of a child, aged $7\frac{1}{2}$, dying from tuberculosis pulmonalis, showed a condition of the tubuli seminiferi like those at birth (Fig. XIV).

There was a pronounced round cell infiltration of the interstitial tissue indicating a chronic inflammatory condition. No interstitial cells of Leydig could be seen. Scarlet stained preparations showed no interstitial lipid granules. A few granules could be seen in the embryonic spermatid cells.

Speculating upon the cause of this arrest, seeing that neither tubercle bacilli nor evidence of tuberculous deposit could be found in the testis, it may be supposed that the child possessed a low vitality and that nature never intended reproduction.

2. *Arrest at Puberty.*

The following are examples of arrest at or soon after puberty :

Boy, aged 16, died of chronic morbus cordis of long standing. The tubules were atrophic and showed miniature development. As in the testis at birth, the tubules were separated one from another by abundant interstitial tissue. There was no evidence of formation of spermatocytes or spermatozoa; in fact, the epithelium retained to a great extent its embryonic character, and there was little evidence of mitosis of nuclei. The membrana propria was thickened, and chronic passive congestion had given rise to an interstitial fibrosis; no interstitial cells could be discovered.

As a contrast the following acute case of morbus cordis may be cited :

A young man aged 21 died suddenly of cerebral hæmorrhage caused by aneurysm due to infective embolism. There was ulcerative endocarditis. The seminiferous tubules are of normal size and are packed together with very little interstitial tissue; normal spermatogenesis with abundant lipid in the interstitial cells, the spermatogonia, and cells of Sertoli.

Chronic disease of long standing before puberty is associated with complete arrest of spermatogenesis at puberty. This fact has been shown by an

important research of Kyrle* on the disturbances of the development of the male generative organs at all ages from birth to adolescence. He has demonstrated the fact that chronic constitutional diseases, such as tuberculosis, are associated with arrest of development. One hundred cases were examined; among these, seventy-six were highly undeveloped; of the remaining twenty-four by no means all were normal; more than half showed distinct under-development. Only ten were certainly normal.

Kyrle states that at the first glance it would seem that the under-development of the testes in chronic tuberculosis was due to the effect of the toxin. He points out, however, that out of thirty-nine dying in the first year of life, twenty-nine had undeveloped testes, but only one of these died of tuberculosis. He thinks this proves that the undeveloped organ is already undeveloped when the individual is affected by the disease.

He concludes that a considerable number of children are born with undeveloped reproductive organs. The development of the whole organism is directly under the influence of the reproductive organs. Individuals with undeveloped reproductive organs have less vital resistance to disease than those with normal reproductive organs. Among the children dying with undeveloped seminiferous tubes far the greater number were physically under-developed. The greater number of those dying in early life had undeveloped testes. Kyrle asks the question whether this is a kind of natural selection by which individuals of little genetic worth are cut off in early life.

CORRELATION OF BIOCHEMICAL AND MORPHOLOGICAL CONDITIONS OF SPERMATOGENESIS.

It has been shown that sections of the testis of a new-born child exhibit lipid granules in the interstitial cells, also lipochrome granules similar in appearance to lutein. Fine lipid granules are also seen in and between the embryonic epithelial cells of the seminiferous tubules. Sections of the testis of a four-months infant show that the seminiferous tubes are about twice the size of those at birth; no lipid granules are seen in the interstitial tissue. The appearances of sections of the testis of a boy aged 11 show almost similar appearances to those at four months; the tubes are not much larger. A few of the tubules show cells with mitotic figures and cells of Sertoli can be seen, but they contain no lipid granules.

Not until puberty and active spermatogenesis has commenced are lipid granules found in the interstitial tissue. Usually large droplets of ruby-red-stained fat are seen aggregated together in this tissue. Fine orange-stained granules can be seen in abundance in the interstitial cells of Leydig, in the spermatogonia, and especially filling the cells of Sertoli. The large droplets are probably lipid, with a greater proportion of unsaturated fatty acid.

* Kyrle, Dr. Josef: Ueber Entwicklungstörungen der Menschlichen Keimdrüsen in Jugendalter. *Wien. klin. Woch.*, November 10th, 1910, No. 45. Aus dem pathologisch. Institute in Wien.

The fact that the lipoid ceased to appear in the interstitial cells as soon as, and as long as, spermatid cell growth ceased and reappeared with active spermatid cell proliferation, may be regarded as very suggestive evidence of the phosphorized lipoid being connected with nuclear proliferation.

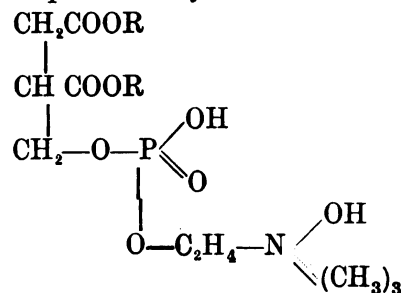
This conclusion, moreover, is supported by the fact that in advanced regressive atrophy the fine orange-stained lipoid granules have almost entirely disappeared from the interstitial tissue.

The cells of Sertoli may in some cases of advanced atrophy still contain lipoid. Only large ruby-red droplets of varying size are usually seen in the very atrophied tubules, which may be explained by a fatty degeneration of the cells.

THE CORRELATION OF BIOCHEMICAL PROCESSES WITH THE HISTOLOGICAL APPEARANCES.

1. In films of seminal fluid from the vesiculæ seminales and sections of the testis stained with a basic and acid dye, such as hæmatoxylin and eosin, Giemsa or Leishman stains, the following microchemical reactions are observed. The head of the normal spermatozoon, consisting of nucleinate, is stained blue by the basic dye. The tail, except the axial thread, stains pink—that is, the lipoid which forms the main constituent of the tail is stained pink.

2. In frozen sections of formalin-hardened testes stained with scarlet dye and hæmatoxylin, and mounted in Farrant's solution to show the distribution of the lipoid granules, the following appearances can be observed. The spermatozoa in the process of development into spermatozoa are stained posteriorly by the scarlet dye and anteriorly by the basic dye. The fine orange lipoid granules are seen in the spermatogonia, spermatocytes, and especially in the cells of Sertoli. The lance-shaped heads of the spermatozoa stained blue are seen diving into the cells of Sertoli, where it may be presumed they behave like living organisms and feed upon the store of lipoid in these "nurse" cells. In situations where sheaves of spermatozoa have attained further development and projected their tails into the lumen of the tube prior to escape as free organisms there is a paucity of fine orange granules observable in the Sertoli cells. Chemical investigations by Miescher and Kossel have shown that the tails consist almost entirely of lecithin and cholesterol with a small amount of protein. Lecithin represented by the formula—



may be looked upon as glycerophosphoric acid combined with choline, a base with the constitution of a tertiary amine, and with two molecules of fatty acids (Koch, 1902).

From the following considerations it appears probable that the phosphorus of the glycerophosphoric acid enters into the formation of the nuclein, a fatty acid being formed which combines with the lecithin continually taken up from the blood and lymph. The presence of the unsaturated fatty acid with the lecithin favours the oxidation processes necessary for the active metabolic processes connected with the cell proliferation (Thunberg, 1909, 1913 ; Warburg, 1913 ; and Warburg Myerhof, 1913).

The "iodine value" indicating the degree of desaturation of fatty acids of lecithins obtained from various organs shows a high figure for lecithin from testicles—117—as compared with 72 for lecithin from ox heart, 81 from liver, and 69 from thyroid (Cruickshank, 1914).

Miescher's experiments show that the tails of the spermatozoa consist largely of a phosphorized fat and some cholesterin, therefore I examined frozen sections of the testicles for cholesterin by Liebermann's test.

The sections were taken out of water, floated on to a slide, a covering glass placed over the section and glacial acetic acid was attracted under the covering glass by the application of filter paper to the edge ; a drop of sulphuric acid was next drawn under the covering glass.

The granules in the interstitial substance and in the circumference of the tubules became pink, and finally turned to green when examined with a magnification of 100. When the magnification was increased to 500 or 600 the fine granules in the spermatid cells, especially the Sertoli cells, were seen to be stained green, also the spermatids and heads of the spermatozoa, which leads me to believe that these active developing cellular organisms have a thin covering membrane containing cholesterol. Seeing that cholesterol is insoluble in cold alcohol, and yet this reagent dissolves out nearly all the substances stainable by the scarlet dye, it follows that the cholesterol, although it has exactly the same distribution as the lipoid which is stained by this dye, must only represent a fraction of the lipoid in which it is in combination.

We know that cholesterol with lecithin enters into the formation of cell membranes. There is good reason, therefore, to suppose that the abundance of lipoid found in the cells of Sertoli during active spermatogenesis may be utilized for forming the tails and covering membrane of the head of the spermatozoa, but the question arises, Is this lipoid substance a phosphorized lipoid and can its phosphorus be utilized in the manufacture of nucleic acid, the principal constituent of the heads ? Wherever there is active cell

proliferation there is abundance of peroxidase granules—that is, peroxidase ferments may be contained in these fine lipoid granules found especially in the syncytial cells.

THE BIOCHEMISTRY OF THE SEXUAL ORGANS.

An excellent account by Cramer of our knowledge of the biochemistry of the sexual organs is given in the admirable work of Marshall, *The Physiology of the Reproductive Organs*, and I shall only briefly summarize the subject in so far as it helps in the arguments relating to the results of my own researches upon spermatogenesis in health and disease.

“According to Slowtsoff, human semen consists roughly of 90 per cent. of water and 10 per cent. solids, which upon incineration yield 1 per cent. of ash.” The solids contain 2.3 per cent. proteins. “In the ash K, Na, Ca, Mg, P, Fe, and S have been found. The quantitative analysis of the ash reveals a remarkably large amount of calcium and phosphoric acid—namely, about 20 per cent. Ca and 30 per cent. P_2O_5 .”

The chemistry of spermatogenesis was first investigated by Miescher, who correlated histological examination of the milts of Rhine salmon with chemical analysis. His histological observations enabled him to separate in bulk the portion of the milt containing the heads from that of the tails. He showed that the chemical composition of the former differed essentially from the latter. Miescher found that the heads consisted chemically of two substances—a highly nitrogenized substance which he termed “salmin,” and a highly phosphorized substance, nucleic acid. The two are in chemical combination and form a nucleinate.

Kossel continued the researches of Miescher, and showed that the heads of the spermatozoa of other species of fish consisted of a combination of these two substances—namely, a protamine which is specific for each fish and nucleic acid which is common to all vertebrates. It was also shown by these investigators that the tails of the spermatozoa consisted of protein, a large amount of phosphorized lipid, and cholesterol in smaller amount.

During the breeding season the salmon takes no food, but feeds on its muscles. The protamine comes from the muscle. It was shown that the blood of the fish during the breeding season contained a large amount of phosphorized lipid, which therefore, in all probability, is utilized in spermatogenesis. This lipid must have come from the muscle or from metabolic processes incidental to the wasting of the muscles.

The researches of Loeb show that the iron of the nucleus of a cell acts as a catalyser, in the presence of oxidase, converting molecular into atomic oxygen—not only may complex substances be split up into simpler substances, but simple substances may be synthetized into complex substances thereby.

The first step in all proliferation is the taking up of the raw material for growth by the living cell ; it is brought to the gland by the blood and lymph channels.

Our previous remarks show that certain elements are especially required—namely, Ca, N, P, Fe. In all active proliferating cells there is oxidase ferment in the form of fine granules, and these, under the influence of the iron catalase in the nucleus, are able to convert the molecular oxygen into atomic oxygen, and the chemical processes which are set in action enable the cell, including its nucleus, to build up substances like unto itself from the raw material brought by the blood and lymph. The first morphological change is visible in the chromatin of the nucleus, karyokinetic figures appear heralding the division of the nucleus and the cell. It is highly probable either that the oxidase granules are lipid substances with a certain amount of unsaturated fatty acid, or they have a lipid film on the surface, the phosphorus having an affinity for the oxygen with which it is in unstable combination, consequently O_2 is readily converted into free atomic oxygen, O , by the catalyser iron of the nucleus.

Some experiments of Cramer carried out in 1908 suggest that these phosphorized fats may act as oxygen carriers, and that they may thus fulfil an important function in all respiration.

That phosphorized fats are in all probability the source of nucleic acid is supported by the following facts. Neither nucleo-protein nor pentoses are present in the fresh egg, and purin bases are only present in very small amounts. During development of the egg these substances rapidly increase in amount, indicating a synthesis of nucleo-proteins from the reserve material of the egg—namely, proteins and phosphorized fats.

Wolfgang Ostwald has determined the amounts of oxidizing ferments present in the testes of toads, frogs, and newts. The watery extracts of these organs had the power of decomposing hydrogen peroxide with the formation of water and oxygen, and of oxidizing guaiaconic acid to guaiacum blue, so that a blue colour appeared when these extracts were added to an emulsion of guaiac resin. These reactions indicate the presence of a catalase and of a peroxidase in the extracts of the sexual glands. Such ferments are present in many, if not all, organs and tissue fluids, but a special significance is attributed by Ostwald to their presence in the ova and spermatozoa.

MICROCHEMICAL TESTS REGARDING THE NATURE OF THESE LIPOID GRANULES.

A phosphorized lipid—for example, lecithin—is stained an orange colour, fat or a fatty acid a deep ruby-red, by scarlet dye. Sections of the medulla oblongata from three cases of death by shock caused by gunshot wounds with compound comminuted fractures of the femur, with fat embolism, showed this remarkably well.

Degenerated nervous tissue, in which there is free fatty acid the result of decomposition of the phosphorized fat (myelin), is stained black by Marchi fluid (1 per cent. osmic acid in 5 per cent. potassium bichromate solution), whereas the myelin of normal nerve is stained an ash-grey. Both these microchemical reactions have been employed in this investigation. I have found that in sections of normal testicle there is invariably within the spermatogonia, cells of Sertoli, and to a much less degree the spermatocytes, an accumulation of fine granules which are stained orange or ash-grey according to the staining reaction employed. Under a low power these granules form a ring within the basement membrane of the tubes (see Figs. VI and VIII), but the interstitial staining by these methods varies very considerably as to the amount of fatty acid and phosphorized fat present in testes where active spermatogenesis is taking place. We may ask the question, Is this variability in the amount of fatty acid present in the interstitial tissue due to a decomposition of the phosphorized fat in the formation of the nucleic acid? But wherever we have this fatty reaction the cholesterol reaction is also obtained, so that it is not a simple fatty acid but a cholesterol combination. The fine orange granules of phosphorized lipoid also give this cholesterol reaction; we must therefore suppose that this substance is present in the granules found in the spermatogenic cells. But cholesterol is present in the tails of the spermatozoa, although in much smaller amount than lecithin; moreover, these two substances form the periplasium constituting the osmotic membrane of the spermatocytes, spermatids, and spermatozoa.

Now the oxidase reaction (in the few cases in which I have employed this test) corresponds in its distribution, both in the interstitial tissue and in the seminiferous tubes, to the scarlet, osmic, and cholesterol reactions—a fact which seems definitely to show a functional correlation between lipoid and oxidases. The following experiment supports the conclusion that these lipoid granules are connected with the oxidation processes.

Small portions of the testis of a freshly killed guinea-pig were placed in a solution of vital methylene blue. These fine granules took up the dye. The tissue was placed in saline solution and covered with a covering glass which was surrounded with vaseline. The preparation was put into the warm chamber. After some hours all the blue colour had disappeared. Upon lifting up the covering glass and admitting the air all the coloured granules reappeared. A clear proof that these granules use up and take up oxygen.

It is an interesting fact that the testes of persons dying from the most varied forms of microbial infection in which toxins must have circulated in the blood and lymph for a considerable time nevertheless show active spermatogenesis. The interstitial tissue and the tubuli seminiferi contain abundant lipoid in the same situations as in cases of sudden death by injury.

Cortex Adrenalis and the Reproductive Function.

There is evidence to show that one of the functions of the adrenal cortex, the cells of which are filled with lipoid substance, is to provide lipoid for the building up of the myelin of the developing nervous system. The evidence in favour of this is as follows :

1. A correspondence in size of the adrenal cortex and the brain in the animal series.

2. The great diminution in size of the adrenals in anencephalous monsters.

But it has other functions—namely, the storage of lipoid—which, as occasion arises, can pass into the blood and keep constant the supply of lipoid to the reproductive organs, where it constitutes the raw material for formative nuclear activity. This functional correspondence of the adrenal cortex and sexual glands is indicated by certain pathological facts—namely :

1. Adenoma of the suprarenal cortex has been found associated with marked sexual precocity.

2. Among my cases an active spermatogenesis in a man aged 69, who died after many years' residence in the asylum suffering with dementia of arrested general paralysis, was associated with a large adrenal cortex.

3. In four male cases of well-marked dementia praecox, with regressive atrophy of the testis, the adrenal cortex was narrow and the cells contained much less lipoid than in other cases of mental disease dying in the asylums. I have only paid attention to this matter lately, but it is being followed up to see if there is a correlation.

4. The cortex adrenalis in the teleostei and elasmobranch fishes is a separate gland. The medullary substance, with its chromaffin, is a part of the sympathetic nervous system.

5. Rats fed upon suprarenal gland showed hypertrophy of the testes ; other organs did not show hypertrophy (Swale Vincent).

6. The cortex adrenalis is developed close to, or forms part of, the genital ridge, and in one case of dementia praecox, where there was only one testicle, the adrenal gland of one side weighed less than one-half that of the side in which the testis was present, and this difference in weight was mainly due to diminished cortex.

I have observed in a large number of cases where the patient has died from a disease in which there has been microbial infection and consequent toxaemia a marked diminution of the amount of stainable lipoid in the adrenal cortex, and I agree with Elliot that this adrenal lipoid probably passes into the circulation to form antitoxins. Now, it is a remarkable fact that however much the lipoid may have diminished, on this account, in the adrenal cortex, it does not seem to have diminished in the testis. Possibly this may account for the fact that, in all manner of chronic microbial infections with toxaemia, active spermatogenesis may nevertheless be seen in the seminiferous tubules. This supports the premise that these lipoids form a protective barrier by virtue of the free atomic oxygen liberated upon their surface ; thus affording a special

provision of nature to protect the germ cells from injury, as well as providing at the same time the oxygen and raw materials necessary for the most fundamentally vital cell activity in the body.

The Oxidase Reaction Applied to the Cortex Adrenalis.—According to Marinesco, the cortex adrenalis does not give the oxidase reaction because the contents of the cells stain uniformly and not as granules, but some cells from which some of the lipoid has escaped do show granules of lipoid and these stain in a similar manner to the granules in the testicles.

THE INFLUENCE OF SYPHILIS ON THE GERM CELLS.

GENERAL PARALYSIS.

Examination of Emulsion of Brain and of Testes by Dark-ground Illumination.

I HAVE examined *post mortem* an emulsion of the brains of a successive series of 100 cases of general paralysis of the insane by dark-ground illumination and found the spirochaete present in 66 per cent. Seeing that the Wassermann reaction can be obtained in the cerebro-spinal fluid in 97 per cent., it is probable that if the search was sufficiently prolonged spirochaetes would be found in a like percentage of cases. My assistant, Mr. Geary, has examined by dark-ground illumination the seminal fluid obtained *post mortem* from the vesiculae seminales of 50 cases of general paralysis, also an emulsion of the testicles; spirochaetes have not been once seen. This result indicated that the seminal fluid of a paralytic is in all probability non-infective at the time he is suffering with this disease. The family history of 54 male tabic or tabo-paralytic patients showed that they had 151 children alive, 75 who were born alive but died in early infancy, and 52 born dead or miscarriages. This offered a striking contrast to the family history of 25 female tabic or tabo-paralytic patients, 10 of whom were sterile; the remaining 15 had 10 children alive, 10 who were born alive but died in infancy, and 51 miscarriages or still-births. But it must be remembered that in the latter case both father and mother are syphilitic, and in the former the father in most instances married when the spirochaete was no longer circulating in the lymph stream of the body, but confined to the specially closed lymphatic system of the brain and spinal cord, the periadventitial sheath of the vessels and perineuronal spaces which contain the cerebro-spinal fluid.

The disease does not arise, on an average, until ten years after infection, consequently if the infected man has not married until five years after, it is unlikely that he will syphilize his wife, and he may, and generally does, procreate and have healthy children, in spite of the fact that he has spirochaetes in his brain and that his blood and fluid give a positive complement reaction.

It is possible that the spirochaetes of general paralysis and tabes have a biological disposition to enter the brain and spinal cord, where they can exist in the tissues and cerebro-spinal fluid away from the attacks of leucocytes and spirochaeticidal agents, such as arsenic and mercury preparations. Förster and Tomaszewski removed tissue containing spirochaetes (living) from the brains of general paralytics, but were unable to infect the testicles of monkeys with them.

Now, examination by dark-ground illumination of the seminal fluid in the vesiculae seminales in cases dying of general paralysis or tabo-paralysis (fifty in number), has invariably shown the existence of spermatozoa, generally in great numbers, even at advanced stages—for example. One case of arrested general paralysis of the insane was 69; also active spermatogenesis may be found in sections of the testes in advanced stages of the disease. The greater number of cases of general paralysis show spermatozoa in emulsions of the testes, proving that there was active spermatogenesis taking place, in spite of advanced brain disease with its accompanying dementia and paresis.

Films of the semen contained in the vesiculae seminales were stained and showed normal staining and normal-shaped spermatozoa; but also varying, yet generally large, numbers of degenerating forms. In some instances the latter were far in excess of the normal, but very seldom did the semen show the same deficiency in numbers of spermatozoa or such degenerated forms as in the semen contained in the vesiculae seminales of cases of dementia praecox, even in comparatively early stages.

Examination of Sections of the Testis.

In several cases there was atrophy of one testis, and this, when examined microscopically, showed patches of degenerated and atrophied tubules only; and pale-staining or eosin-staining empty shrunken tubes were seen; all the spermatogenic cells had disappeared in these patches, leaving only the thickened membrana propria and sustentacular framework. Between the tubules are seen the interstitial cells, and these may form nodules or islands amidst the degenerated empty tubules (Fig. XV). The cause of these patches of degenerated tubules may be some obstruction of the vasa efferentia from an old gonorrhoeal epididymitis, old local syphilitic inflammation, or arterial sclerosis, for the same appearances were found in a well-marked case of generalized arterial sclerosis.

We may conclude therefore that an acquired dementia, due to the direct action of the toxins of the spirochaetes of syphilis on the brain, even though the destruction is great, does not cause any generalized arrest of spermatogenesis. Many of these cases had died with advanced tuberculosis, others had died of

bronchopneumonia or dysentery, and yet active spermatogenesis existed in many of the tubules.

These results are of interest when taken into consideration with the results of severe injury of the brain and spinal cord, followed by prolonged sepsis and suppuration, where arrest of spermatogenesis was sometimes observed. It may be assumed that extensive destruction of the brain or a severe lesion of the spinal cord, with prolonged sepsis and pus formation, can arrest spermatogenesis, whereas a slow insidious progressive destruction of the higher cortical structures spread over years, but without prolonged suppuration, will not do so. The arrest of spermatogenesis is probably due to the prolonged suppuration entailing the using up of lipoids.

CONGENITAL SYPHILIS.

Congenital syphilis may affect the testis in various ways. The spirochaetes may invade the testis in common with other organs of the body, as in the following case of fatal prenatal syphilis.

1. A dead full-term fetus from Shoreditch Infirmary was examined. All the tissues including the testis, were found to contain spirochaetes. The invasion of the testis was, probably recent and due to a spirochaetal septicaemia. Sections of the organs stained by Levaditi's method showed abundance of spirochaetes, many undergoing plasmolysis. There was some degree of inflammatory change, and this has produced a condition by which the groups of interstitial cells of Leydig were only indistinctly seen compared with the normal. Their outline is very indistinct and the cytoplasm appears to be disintegrated and vacuolated. The fibrous tissue is increased and there is an abundance of lymphocytes. It is probable that if this child had survived and lived to adolescence there would have been a complete arrest of development of the tubules and interstitial cells and probably partial or complete destruction of the same, with replacement by dense fibrous tissue.

The accompanying pedigree chart was made by Miss Agnes Kelly, who conducted for the Board of Control an investigation of families in Bethnal Green. It will be observed that she has obtained no syphilitic history in this very degenerate stock. The pedigree

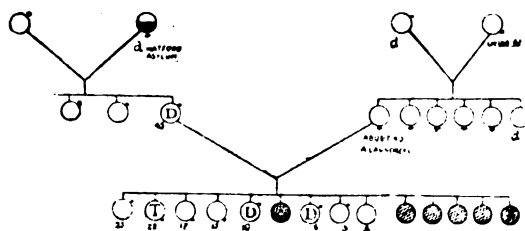


FIG. XVI.

FIG. XVI.—Pedigree of a degenerated stock. The father, D, was a drunkard degenerate, married a woman of fairly healthy stock; thirteen conceptions, the last five being miscarriages. The final was the case in which premature birth occurred, in which the spirochaetes were found in all the organs of the body including the testes. The four previous miscarriages were no doubt due to syphilitic infection of the mother. No history of syphilis was obtained by the investigator of this pedigree, but this objective proof demonstrates that syphilis was the cause in the previous cases.

chart shows that there were five offspring successively dying in infancy, attributed to teething, convulsions, and consumptive bowels (Diagram Fig. XVI). Observation shows that spirochaetal infection was the cause of this infantile mortality and possibly the previous degenerate and diseased offspring might be accounted for by a syphilitic father and mother ; although it is more likely the mother became infected after the ninth conception.

2. In a congenital syphilitic child, aged 4 months, from Shoreditch Infirmary, with syphilitic rash on the body, dead of pneumonia, the tubuli seminiferi were twice as large again as in the newborn child. The interstitial cells are present and contain lipid, but they are relatively few in number compared to the testis at birth. There are fine lipid granules seen in the epithelial cells of the tubules. In this case the spirochaetes have not invaded the testicles. Consequently there is no arrest of development and the appearances are normal (Fig. II).

Juvenile General Paralysis.—H. L., aged 8, was brought by his mother to Charing Cross Hospital. He was a typical congenital syphilitic. The mother had had miscarriages and children born dead before he was born. The patient suffered with a gummatous node on the right arm ; there was paralysis of the left external rectus ; choroido-retinitis ; Hutchinsonian teeth and well-marked rhagades round the mouth ; he snuffled and was stunted in growth. He was treated with mercury. The mother came and told me later that her boy had had a fit at school. He had passed a motion during the fit ; prior to his losing consciousness he was seen to be writing, and rubbing out what he had written on his slate in a strange manner. He was a good boy, but backward at school. I lost sight of him for eight years, when I found him in Colney Hatch Asylum, suffering with juvenile general paralysis. Although 16 years of age, he was in bodily growth and mental development like a boy of 8. There was no hair on the pubes, the genital organs were very small. The testes were infantile in size. The boy died after a few months' residence in the asylum. The brain showed a very advanced condition of dementia paralytical. No doubt the fit he had eight years previously was due to an active spirochaetal development in the brain. Now the testes in this case were not larger than small filberts ; examined microscopically, they showed a complete arrest of development of the tubuli seminiferi (Fig. XVII). They were no larger than those at birth ; there was a round-celled infiltration of the interstitial tissue, but no cells of Leydig could be seen. Preparations stained with osmic acid showed no interstitial lipid. It is possible that there had been a spirochaetal invasion, as in the case of C., or it may be that the syphilitic toxæmia, which had persisted from birth, had had a devitalizing influence and caused the arrest.

A. B., admitted to Colney Hatch at the age of 21. Diagnosis epileptic. He was sent to the colony at Ewell, but transferred to Claybury on account of outbursts of violence, attended by excitement, and associated with progressive dementia. He was diagnosed as epileptic dementia, and it was not until he died and was examined by me on the *post-mortem* table that the true nature of the disease was discovered. I found an old leukoma on the right cornea, but this was the only obvious symptom of congenital syphilis observable. The cerebro-spinal fluid was drawn off *post mortem* by lumbar puncture and an abundance of lymphocytes found ; a marked positive complement deviation of the fluid was obtained. There was a marked excess of fluid in the lateral ventricle, and the fourth ventricle was very granular. The right hemisphere weighed 30 grams more than the left ; the convolutions generally were atrophied, and the membranes were thickened and adherent, especially over the mid line, so that I came to the conclusion that this was a case of congenital syphilis and juvenile general paralysis of the insane of slow development. The

seminal fluid in the vesiculae, diluted with pericardial fluid, showed an abundance of normal shaped spermatozoa, some of which were still active eight hours after death. The right testis weighed 20 grams; the left 8.5 grams. Emulsion of each showed spermatozoa.

Microscopic examination of films of the seminal fluid stained with haematoxylin and eosin showed normal stained spermatozoa, with very few degenerate forms. Sections of testis stained with scarlet showed an abundance of interstitial lipid; there was also a fair amount of medium-sized and fine orange granules in the spermatogonia and cells of Sertoli. Here and there were patches of ruby-red, irregular masses of droplets and granules corresponding to the situation of completely degenerated tubules. Haematoxylin and eosin preparations of the left testicle showed a number of tubules with thickened basement membrane. Lying inside were cells of Sertoli and vacuolated degenerated spermatogonia. The greater number of the seminiferous tubes appeared to be perfectly normal, showing normal spermatogenesis in all stages. A few spermatozoa could be seen in some of the atrophied tubules. The most advanced stages of degeneration of the testes exhibited tubules with thick basement membrane and the lumen filled with an amorphous matter stained by the eosin dye. The interstitial cells appear to be normal in these degenerated areas.

H. A., aged 23. Admitted to Claybury March 2nd, 1914, diagnosed as dementia tabo-paralytica, died June 26th, 1914. Brain meninges thickened and opaque, granular fourth ventricle. Naked-eye sclerosis of posterior columns.

Examination for Spirochaetes.—Right and left temporal lobes few, left mesial frontal numerous, left frontal lobe fairly numerous, also motor area. None in spinal cord. Not only were spirochaetes found in these regions by examination with dark-ground illumination of emulsions of the brain, but in films stained by Fontana method. Emulsions of the testicles were examined by the dark-ground illumination; a few spermatozoa were found, but no spirochaetes.

Sections of the testes show some tubules with spermatozoa and active spermatogenesis in all stages; far more, however, show an arrest of development with thickening of the basement membrane. Sections of material hardened in Flemming's solution show interstitial lipid and fine granules of lipid in the cells of Sertoli.

A. R. able-bodied sailor, R.N., aged 21. Father died of general paralysis of the insane. Mother demented. No signs of syphilis on the body visible, but his brothers showed well-marked signs. A younger brother (imbecile), who was in Caterham Asylum, was a well-marked congenital syphilitic. This patient was in the navy, and developed general paralysis with epileptiform seizures, in one of which he died. Although there was no obvious external signs of congenital syphilis, the liver showed marked pericapsular, perivascular and pericellular fibrosis. The brain showed the characteristic lesions of general paralysis of the insane. The testes weighed together only 20 grams but showed active spermatogenesis in many of the tubules.

Sections stained with haematoxylin and eosin show patches of atrophied tubules in which the whole of the epithelium has disappeared, and in these places there is a marked increase of connective tissue. Where the connective tissue is of normal amount the seminiferous tubules are larger and packed close together. These tubules show all stages of active spermatogenesis. These are a large number of lymphocytes in the interstitial tissue where the atrophied tubules are seen. This may have been caused by a localized spirochaetal colonization. The interstitial hormone cells do not seem to have been destroyed, however. The interstitial cells contain lipid; and lipid granules are seen in the spermatogonia and Sertoli cells.

The Relation of Congenital Syphilis to Infantilism.

Infantilism, as was long ago pointed out by Fournier, is a frequent condition met with in congenital syphilis, and I have seen a large number of cases of juvenile general paralysis of the insane affecting the male sex in adolescence in which there was an infantile condition of the genitalia, absence of pubic hair, absence of hair on the upper lip and chin, a treble voice, stunted growth—in fact, a failure in the appearance of the secondary sexual characters.

In only one of the four cases here recorded (H.I.) was there infantilism. Examination of the testes showed an infantile condition of the tubules and *a disappearance of the interstitial cells*. The other three cases all showed plenty of interstitial cells—hence the secondary sexual characters were present.

There can be no doubt that syphilis in the parents may lead to infantilism in the offspring, and I have seen numerous cases of infantilism in which there was no obtrusive signs of syphilis, although other children of the same parents presented well-marked stigmata; moreover, cases show that one individual of a family of congenital syphilitics may exhibit the characteristic stigmata of congenital syphilis and another show no external signs, yet the internal organs may exhibit *post mortem* the most marked evidence of the disease. I have, as previously stated, found spirochaetes in the brain of a juvenile general paralytic who showed no external sign of congenital syphilis, and who during life was regarded as a case of epileptic dementia, the true nature of the disease having been discovered *post mortem*. Are we, then, to consider that every case of infantilism in congenital syphilis is caused by spirochaetal invasion of the testis, or is it not more likely due to the effect of a chronic spirochaetal intoxication depressing the vital energy of the whole body, as in chronic juvenile tuberculous cases?

It would be of interest to examine the pituitary gland in these cases for the spirochaetes which have caused the brain disease. Some cases, as that of R., in which there was extensive perihepatitis and pericellular fibrosis, evidence of a past active spirochaetosis of the internal organs, nevertheless manifested no infantilism.

Examination of the testicle showed that if a spirochaetal invasion had occurred the resultant inflammatory change had caused only a local and partial destruction of the gland. Some of the seminiferous tubules showed an extreme atrophic change with destruction of the whole of the spermatogenic cells, only the membrana propria remaining, but in the immediate neighbourhood were normal spermatid tubules showing active spermatogenesis; the interstitial cells were present in abundance in the atrophied areas. Three of these cases of congenital syphilitic dementia paralytica showed in every way the same histological appearances met with in a large number of cases of

paralytic dementia due to acquired syphilis. The histology of the testis and vesiculæ showed they were capable of procreating. What would be the influence on the offspring? All the evidence tends to show that every syphilitic child has a syphilitic mother. I have only seen one case of congenital syphilis transmitted to the next generation.

CONGENITAL IDIOCY OR IMBECILITY WITH EPILEPSY AND SPERMATOGENESIS.

The testes were obtained from the subjoined five patients dying in Caterham Asylum. The material was kindly sent to me by Dr. Campbell, the superintendent. There was one case also dying in Claybury investigated. All the patients were unmarried, and the history as to heredity was unknown.

CASE 1.

E. W. S.; age on admission 23. Had been an imbecile, with epilepsy, from birth. Died from pulmonary tuberculosis, peritonitis, and enteritis, on March 26th, 1912, aged 32.

Autopsy (March 27th, 1912).—The brain weighed 44½ oz.; there was no deficiency of development of the cerebral convolutions (symmetrical); no gross lesions. Weight of testicles: Right, 18 grams; left, 15 grams.

CASE 2.

H. M.; age on admission 16. Had suffered from idiocy with epilepsy from birth. Died, aged 19, on April 9th, 1912; the cause of death was enteritis, the other organs being normal.

Autopsy (April 12th, 1912).—The brain weighed 30 oz.; there was general deficiency of development. Weight of testicles: Right, 3½ grams; left, 2.8 grams.

CASE 3.

H. A.; age on admission 17. Had suffered from idiocy, without epilepsy, from birth. Died, aged 21, from pulmonary tuberculosis, on April 19th, 1912.

Autopsy (April 20th, 1912).—The brain weighed 43 oz.; there was opacity of the pia arachnoid, considerable accumulation of fluid, and general deficiency of development. Record of the weight of the testicles before preservation were lost; 4.5 grams and 3.2 grams respectively after hardening in Müller, October 18th, 1915.

CASE 4.

W. C.; age on admission 18. Had been an imbecile from birth, but without epilepsy; no arrest of spermatogenesis. Died on June 2nd, 1912, of lobar pneumonia with cardiac dilatation, aged 44.

Autopsy (June 4th, 1912).—The brain weighed 42½ oz.; there was deficiency of development of convolutions with commencing atrophy. Weight of testicles: Right 20 grams; left, 23 grams.

CASE 5.

J. D.; age on admission 15. Suffered from imbecility, with epilepsy, from birth. Died on June 2nd, 1912, at the age of 16; the cause of death being the status epilepticus.

Autopsy (June 4th, 1912).—The brain weighed 45½ oz.; there was congestion of the meninges, marked increased vascularity of cortex, basal ganglia, and cerebellum, and deficiency of development of convolutions. Weight of testicles: Right, 12 grams; left, 11 grams.

CASE 6.

J. R. Y., a congenital imbecile, was 31 years of age on admission to Claybury ; he died of lobar pneumonia, aged 51.

Autopsy.—The brain weighed 1085 grams ; each hemisphere only weighed 475 grams. The pons, medulla, and cerebellum only weighed 120 grams. The testes were very small and atrophied ; no sign of spermatogenesis.

Cases 1, 2, 3, and 5 all showed a complete arrest of spermatogenesis.

Cases 1, 2, 5, and 6 showed arrest of development of the seminiferous tubes, no evidence of karyokinesis of the nuclei of the cells and a very thickened *membrana propria*.

In Case 2, with very marked fibrotic atrophy the tubules are hardly discernible in the dense fibrous tissue ; where cells are seen in the tubules they are either embryonic in appearance, or more usually they are either degenerated or destroyed, and completely replaced by a hyaline swollen mass, staining pink with eosin as if coagulation necrosis had occurred. So complete and universal is the pathological change that it is difficult to recognize the organ as testicle.

In only Case 1 could I find any normal interstitial endothelial cells, and these existed in characteristic groups and contained lipid granules.

In Case 4—imbecility without epilepsy—there was no naked-eye abnormality of the testis, the weights were normal, and sections of the organ exhibited active spermatogenesis.

Cases 2 and 3—idiots—show the most marked changes in the testes (Figs. XVIII and XIX).

These observations appear to show the influence of congenital epilepsy in completely arresting spermatogenesis, although not necessarily, as in Case 1, affecting the interstitial cells. It may not, however, be due so much to the occurrence of the fits as the morbid condition which has caused the fits. The appearances rather suggest congenital syphilis as the cause. Probably Case 4 was a higher grade imbecile, and the examination of the testes shows that these individuals are, from a eugenic point of view, the most dangerous to the community.

SPERMATOGENESIS IN DEMENTIA PRAECOX.

When dementia praecox manifests itself at puberty or early adolescence the morbid histology of the testis may present a different picture from that seen when the disease commences in adolescence and after the sexual glands have become functionally active. There may be an arrest of development of the seminiferous tubes.

It is often difficult to determine precisely the age of onset of many cases of dementia praecox. Doubtless many of them had really manifested pre-

monitory symptoms years before they were certified and sent to an asylum. Indeed, as Kraepelin points out, some of the cases have commenced in early childhood. They are, in fact, cases of dementia precossissima. So it is not possible to correlate accurately the duration of the clinical symptoms with the degree of regressive atrophy of the testis. As a general rule it may be said, as regards those in which the symptoms commenced in adolescence, that the longer the patient has been in the asylum the more pronounced is the morbid change in the testes.

Eight cases were investigated in which the disease in all probability commenced in early adolescence, and twelve in adolescence or later. Besides those twenty cases which died in the London county asylums the material from two cases was also received from Dr. Turner of Brentwood; both these latter had only manifested symptoms a relatively short time.

The size and weight of the testicle did not always correspond with the degree of change in the organ, and this may be accounted for by the fact that in some cases the interstitial fibrous tissue is more increased than in others. As a rule, however, large testes were more likely to exhibit spermatogenesis than small ones. The testes with regressive atrophy showed, as a rule, no spermatozoa when an emulsion was made of the organ and microscopic examination by dark-ground illumination effected. There is usually a correspondence between the naked-eye and the microscopic changes in the testes.

The contents of the vesiculæ seminales in the cases in which they were examined were either devoid of spermatozoa or the spermatozoa were markedly degenerated in all but the earliest stages of the disease. (Compare Figs. XI and XII and XXVII.)

Morbid Histological Changes in the Testes.

Microscopic examination of the testes reveals three stages of regressive atrophy in sections stained with haematoxylin and eosin or van Gieson.

Stage I. (Well exemplified in three cases.)

Many of the tubules are considerably diminished in size and contain no spermatozoa (Fig. XX); spermatogenesis is seen in only a few of the tubes relatively to the normal; the spermatocytes are fewer in number and their nuclear staining is not so good, mitosis and karyokinetic figures in the spermatocytes are not so well seen and the nuclear skein of active mitotic division is less evident. The formation of spermatids is either not evident in the tubules or less than in the normal tubules. The cells of Sertoli which in the normal tubules are crowded with lipoid granules, forming a syncytium which fills up the spaces between the spermatogonia and spermatocytes, are in the atrophied tubules empty, or partially empty, thus rendering them distinctly visible (Figs. XX and XXI). The basement membrane is thickened and,

instead of consisting of one layer of nucleated flattened cells, consists of several layers. The nuclear substance of the spermatogenic cells stains with a variable degree of intensity with the haematoxylin. Indeed, one of the most obvious signs of regressive atrophy is a diminution of stainable nuclear substance. (Compare the appearances of Figs. XIX and XX with Figs. V and IX.)

First Stage of Regressive Atrophy.

It is difficult to observe the earliest changes of the first stage, and it is only by a systematic examination with an oil-immersion lens and comparison with normal sections stained in a similar manner that changes can be determined.

Some of the tubules may show normal spermatogenesis, and it may be that a patient may suffer with the signs and symptoms of dementia praecox* and have normal testes.

I have already stated that the vesiculae seminales may contain abundance of degenerated spermatozoa and that this degeneration may be recognized by their staining reaction—for example, the head stains throughout with the eosin and not with the haematoxylin. It may be assumed that this staining indicates that these spermatozoa have long been dead. In sections of the testis of cases diagnosed as dementia praecox* which die within a year or two of the onset of symptoms active spermatogenesis exists in many of the tubules and numbers of spermatids and spermatozoa may be seen; when these are examined with a high-power magnification, a large number of the spermatids, however, do not appear sufficiently stained with the haematoxylin, but are largely stained with the eosin. Again, the heads of the young spermatozoa are similarly imperfectly stained with the haematoxylin, and a large number are stained throughout pink with the eosin, indicating a degenerating condition. These spermatozoa, moreover, do not seem to penetrate into the cells of Sertoli to grow and develop their tails as occurs in the normal. It is not claimed, however, that a colour reaction alone is a convincing proof of commencing degeneration (Fig. XXVI).

Again, in places the tubules, although containing numerous spermatocytes and spermatogonia, show a deficiency of nuclear matter, for the mitosis and kinetic figures are absent in some of the cells and in others are not so well marked or are deficient. Where these appearances in the tubules occur the cells of the membrana propria have proliferated. In most of the tubules, however, the cells of Sertoli in these early stages show abundance of lipid granules.

* It may be mentioned that non-degenerative forms of dementia praecox are occasionally met with, and it is not always easy to diagnose dementia praecox in the early stages. Cases of confusional insanity may present a similarity in clinical symptoms to dementia praecox. As Régis points out, chronic confusional insanity may terminate in dementia.

- These early changes are, as a rule, found in cases in which symptoms of the mental affection have not been long manifest. But I have quite recently had a case with a history of masturbation of ten years' duration in which active spermatogenesis was found in many of the tubules. This patient was an ex-driver in the Field Artillery and died six months after his admission to an asylum from pachymeningitis haemorrhagica. While in the asylum he presented a typical clinical picture of dementia praecox. He had suffered with a penetrating gunshot wound of the head in the frontal region, and there was a generalised chronic perivascularitis, a condition not met with in dementia praecox. It appears probable that his mental symptoms were really due to this rather than a primary degenerative process.

Many of the patients affected by dementia praecox are known to be excessive masturbators, and it might be assumed that the changes are caused by this act entailing a continuous loss of nuclear substance. But there are many arguments which can be advanced against this—namely : (1) In many of the cases the notes do not give this history ; (2) I have pointed out the fact that general paralytics and men suffering with other insanities and neurasthenia, in which prolonged masturbation has occurred, do not exhibit a similar morbid change such as is found in the second and third stages to be presently described ; (3) regressive involutional changes in the ovaries with atretic corpora and degenerated follicles containing dead ova have been described by Dr. Laura Forster in a number of cases of dementia praecox, and this has been confirmed in a case investigated by Dr. Kojima. I therefore agree with Kraepelin that loss of seminal fluid by masturbation is not the cause of dementia praecox, for this mental disease is as common in women as men, and this argument would not hold for women who masturbated continuously. All the evidence points to a degenerative condition.

The Lipoid Reaction.

In the first stage abundance of interstitial lipoid granules are seen ; the syncytial cells contain fine lipoid granules, but in the tubules in which there is regressive atrophy occurring, the fine granules are not equally distributed as a continuous circle in the spermatogonia and syncytial cells.

Second Stage of Regressive Atrophy.

In the second stage the great bulk of the tubuli seminiferi are atrophied and the basement membrane thickened. In relatively few of the tubules are any spermatozoa found. Most of the tubules, however, show spermatogonia and spermatocytes, the latter exhibiting little evidence of active mitosis and formation of spermatids by heterotypical division. In some of the tubules there is evidence of a complete degeneration of the spermatogonia and spermatocytes, the cytoplasm of the cells is swollen and clear, and the nuclei uniformly stained exhibit no evidence of karyokinesis. The interstitial tissue is increased.

Scarlet-stained preparations show abundance of coarse, deep-red lipoid granules in the interstitial tissue. Some fine granules are seen in the syncytial cells mingled with large, irregular sized, coarse, deep red granules in the outer and inner layers of cells of the atrophied tubules. This is in great measure due to a fatty degeneration of the spermatic cells.

Third Stage of Regressive Atrophy.

In this stage the appearances are like those of the second stage only more advanced, and resemble those described in sections of atrophic testicles of two demented octogenarians (vide Cases, p. 12).

The third stage of regressive atrophy is often found in the testes of patients dying in early adolescence, and it is probable some of these were cases of dementia precossissima and spermatogenesis had never occurred.

With haematoxylin and eosin stain the sections show a very marked increase of interstitial fibrous tissue, the cells of Leydig are not distinctly seen.

The basement membrane is markedly thickened, consisting of three or four layers of flattened cells. The cells contained in the tubules may consist of a single or double layer of round cells with clear swollen cytoplasm and round uniformly stained nuclei which exhibit no evidence of karyokinetic figures or active mitosis. In many of the tubules there is nothing left except a few irregular-shaped nuclei and sustentacular threads (Figs. XXII and XXIII).

Scarlet-stained preparations show no fine orange lipoid granules in the syncytial cells, but numbers of coarse and fine ruby-red granules of varying size within the thickened basement membrane, filling up the lumen of the tube (Figs. XXIV and XXV). Obviously these are the products of fatty degeneration of the cells and provide evidence of the last stage of degenerative regressive atrophy.

The above described histological examination of the testes in dementia praecox tends to show that a precocious senility of the germ plasma is a fundamental biological condition in this disease.

Why should this Degeneracy come on in Adolescence?

If we look at the matter from a broad biological standpoint, and consider that Nature is unmindful of the individual and mindful only of the species, it will be obvious that a progressive degeneration of the most vital tissue of the body at an early age would stop procreation of a degenerate stock by anticipation.

Likewise the examination and atrophy of the testes with suppression of spermatogenesis in idiots and imbeciles may be regarded as evidence of the same provision of Nature to eliminate degenerates and thereby support the survival of the fittest. Unfortunately, high grade imbeciles are very fertile,

and serve as a constant source of fresh degeneracy. Space prohibits me from doing more than summarizing the investigation of the male sexual organs in dementia praecox. The essential change in the central nervous system is a degeneration of the nucleus of the neuron, and in all probability a diminution of the organic phosphorous in the cell. This nuclear degeneration is not limited to the cortex cerebri, but is found in all regions of the brain, although in varying degree in different situations in different cases. A full account of the cases will be published in a separate monograph, in which an attempt will be made to correlate the biochemical changes in the sexual organs and the central nervous system in explanation of the disordered psychic functions of this degenerative demential disease of adolescence—a disease which we have seen offers a marked contrast to paralytic dementia, which we know to be due invariably to spirochaetal infection, resulting in chronic inflammatory reaction.

SUMMARY.

1. The testes were examined in 100 cases of deaths occurring at all ages from birth to 86 in London asylums and various civil and military hospitals. The fluid contained in the vesiculae seminales was examined in a considerable number of these cases, and in a few of the cases—especially dementia praecox cases—the thyroid, adrenals, and pituitary glands were also examined.

2. The development of the testis from birth to puberty was studied in a number of cases, with the following results ; At birth there is a large amount of interstitial tissue between the seminiferous tubules ; the interstitial cells of Leydig are observable in great numbers and have the appearance of a gland ; these cells contain a lipochrome substance like lutein and lipoid granules. At four months the tubules are twice the size ; the interstitial cells are hardly visible and there are no lipoid granules seen. At eleven there is very little change in the size of the tubules and the interstitial cells are only discernible by examination with an oil-immersion lens (resting stage). There is little or no interstitial lipoid seen. There are commencing evidences of nuclear activity and karyokinetic figures, but no spermatids nor spermatozoa.

At fifteen (puberty) the tubules are closely approximated and all stages of active spermatogenesis are observable. There is abundant interstitial lipoid, and lipoid granules are seen in the cells of Sertoli, but not so abundant as in the adult.

3. Cases dying before puberty of chronic diseases—for example, tuberculosis, congenital syphilis, and chronic morbus cordis—show appearances of complete arrest of development of the seminiferous tubules. Probably Kyrle's view is correct, that arrested development of the tubuli seminiferi is a sign of deficient vital resistance to disease.

4. Normal spermatogenesis was studied in cases of death from shock caused by severe injuries. Active spermatogenesis is seen in all stages. The interstitial cells contain abundant lipid and the spermatogonia, and especially the Sertoli cells lining the tubules, are filled with fine lipid granules.

5. Where there are sheaves of spermatozoa these granules in the Sertoli cells are less numerous. The immature spermatozoa dive into the Sertoli cells and there acquire their tails, which consist almost entirely of lipid, lecithin and some cholesterin.

6. Evidence is given to show that the lipid granules seen in the interstitial tissue and in the cells lining the basement membrane of the tubules constitute the raw material from which the nucleic acid, necessary for active nuclear proliferation and spermatogenesis, is formed. These lipid granules give the oxidase reaction owing to the presence of traces of unsaturated fatty acid. Decomposition and recombination processes are brought about by the catalytic action of the iron of the cell nucleus upon the oxidase, causing molecular oxygen O_2 to be converted into free atomic oxygen $O\cdot$ on the surface of the granules.

7. Reasons are given for supposing that these lipid granules are derived from the lipid store in the cortex adrenalis. Elliot's work, showing that the lipid content of the cells of the cortex adrenalis is diminished in microbial intoxication, is confirmed. However much it is diminished on this account, the lipid granules in the testes are not appreciably so. This may explain the fact, so frequently observed in this inquiry, that prolonged microbial toxæmia does not arrest spermatogenesis. It seems as if the lipid substance in the testes acted not only as the phosphorized raw material of nuclear activity, but as a protective barrier to the effects of circulating microbial poisons.

8. The spermatozoa in the vesiculæ seminales were observed alive and active eight hours after death in two cases, but the majority were dead. Examination of the seminal fluid from a large number of vesiculæ showed several important facts. In a healthy man the heads of the spermatozoa are stained by the basic dye, whereas in persons dying of various chronic diseases the majority of the spermatozoa are stained by the acid dye indicative of a death change. May not this indicate a survival of the fittest in the vesiculæ seminales and a protective provision of Nature? The most marked degenerative changes in the spermatozoa were found in dementia præcox.

9. Whereas in 66 successive cases of general paralysis spirochaetes were found in an emulsion of the brain, spirochaetes were not once found in 50 cases in which an emulsion of the testis was examined microscopically by dark-ground illumination. This fact may be correlated with the fact that general paralytics, unless the wives are infected, have healthy children.

10. The testes of a large number of general paralytics, including four of the juvenile form, were examined. In only one of these cases was there a complete arrest of spermatogenesis. In many cases there was very active spermatogenesis and normal staining spermatozoa in the seminal fluid. A considerable proportion of the testes, however, showed strands and islands of completely atrophied tubules amidst normal tubules. Seeing that where this atrophy occurred islands of normal Leydig cells are seen, it must be concluded that the atrophy of the tubules was due to local obstruction of the vasa efferentia by gonorrhoea or syphilitic inflammation. In one case of juvenile general paralysis in which the secondary sexual characters had not developed the testes were infantile in development.

11. The testes of 22 cases of dementia praecox were examined. Three stages of regressive atrophy are described for convenience and brevity, but they all gradually merge from the earliest change in the biochemical reaction and morphology of the heads of the spermatozoa to a complete regressive atrophy of all the seminiferous tubules, so that the appearances of the organ as regards capacity for function in an adolescent was less than that observed in the decrepit dement of 86. Indeed, the testis of an old dement of 80 showed more microscopic evidences of virility than many, of the earlier cases, of dementia praecox. In one-half at least of the cases there was complete regressive atrophy. It is possible that this regressive atrophy of the testes may be correlated with a deficient vital resistance to infective disease, especially tuberculosis, from which the vast majority of these cases die.

12. The testes of 6 cases of imbecility and idiocy were examined ; 5 of the 6 showed complete absence of spermatogenesis. Various other forms of mental and bodily disease at varying ages showed active spermatogenesis, in spite of the most advanced and active tuberculosis, dysentery, bronchopneumonia, and gangrene of lung.

13. A full account of the microscopic and biochemical changes in the reproductive organs and the central nervous system in dementia praecox will form the subject of a future communication.

14. There is abundant evidence to show that whereas, on the one hand, the degenerative changes in general paralysis obvious to the naked eye in the brain are due to a chronic inflammatory reaction occasioned by spirochaetal poison ; on the other hand, dementia praecox is a primary nuclear degenerative process with no inflammatory reaction and no obvious naked-eye changes of the brain. An attempt will be made later to correlate the morbid biochemical changes observed in the reproductive organs with those in the brain in this disease.

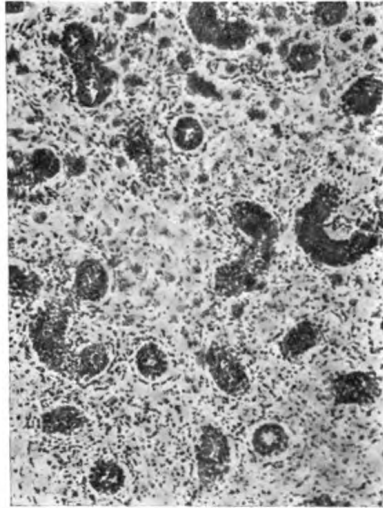


FIG. I.—*Testis of Twin Fetus.*
(Mag. 105.)

To the right between the tubules in the interstitial tissue are seen numbers of polygonal cells. These are the cells of Leydig.

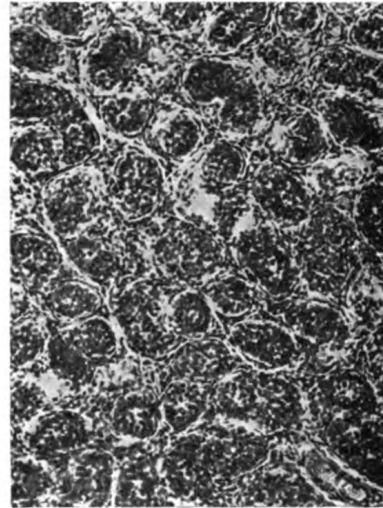


FIG. II.—*Testis of Infant aged 4 Months.*
(Mag. 105.)

The tubules have increased to nearly double the size; the interstitial tissue was correspondingly diminished. The cells of Leydig are not visible.

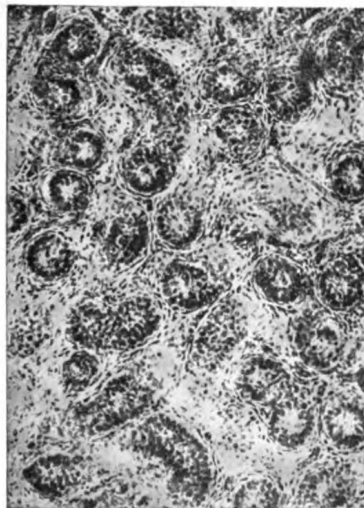


FIG. III.—*Testis of Child aged 3 Years*
(Mag. 105.)

The tubules are smaller than in Fig. II. The cells of Leydig are not seen. There is much more interstitial tissue than in Fig. II.

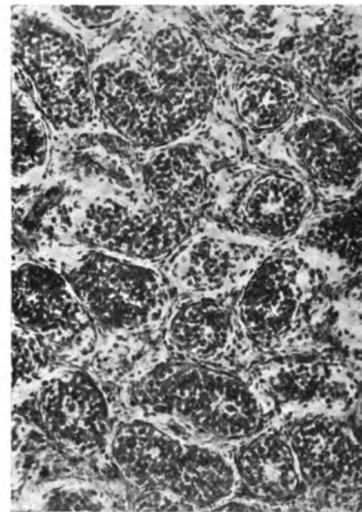


FIG. IV.—*Testis of Boy aged 11 Years.*
(Mag. 105.)

The tubules are larger than in Fig. II. The tubules are approximated. There is a small amount of interstitial tissue. The cells of Leydig are not visible.

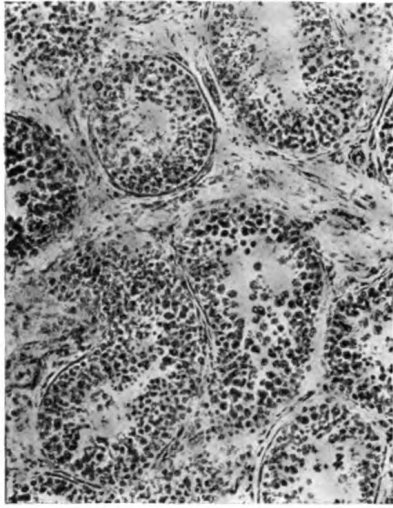


FIG. V.—*Testis of Boy aged 15 Years ; died of Injury.* (Mag. 105.)
The tubules show active spermatogenesis. The fine black dots are the heads of spermatozoa.

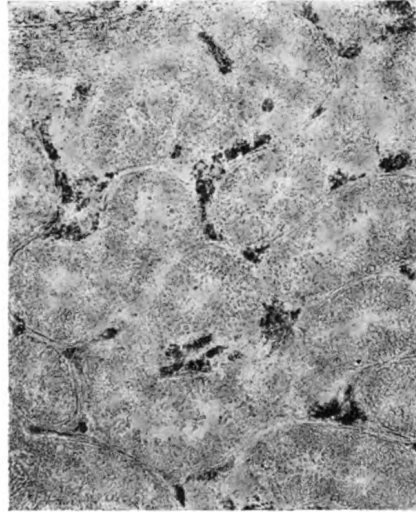


FIG. VI.—*Testis of Boy aged 15 Years ; died of Injury.* (Mag. 70.)
Scarlet-stained preparation to show lipoid. The interstitial lipoid (black) is very well shown. Compare the staining of the tubule with the adult, Fig. VIII.

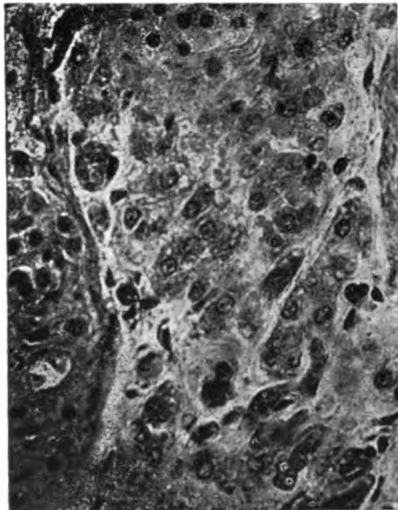


FIG. VII.—*Testis of Adult aged 24 Years ; died of Injury.* (Mag. 385.)
Portion of spermatic tubule, with four heads of spermatozoa seen. To the right is a large collection of cells of Leydig, polygonal in form and with a large round nucleus.

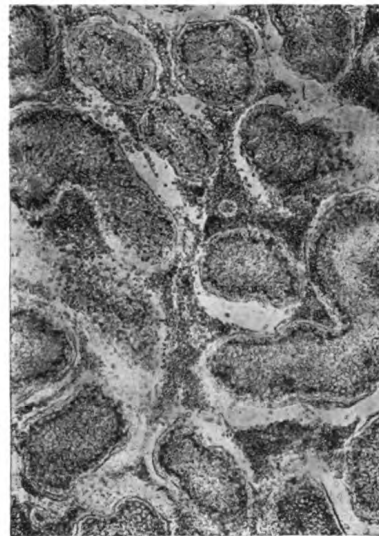


FIG. VIII.—*Testis of Adult ; died of Injury.* (Mag. 70.)
Scarlet preparation showing abundant interstitial lipoid which appears black. Observe also the black zone beneath the basement membrane. This is due to the spermatogonia and cells of Sertoli being filled with lipoid.

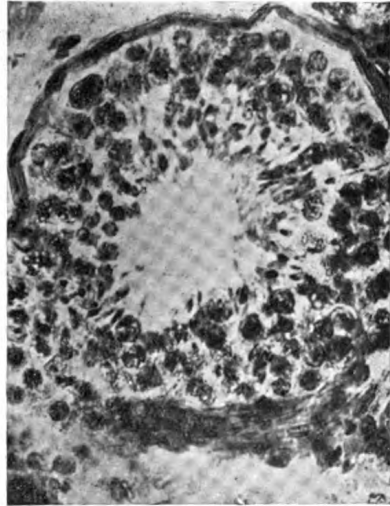


FIG. IX.—*Testis of Adult; died of Injury. (Mag. 376.)*
 Transection of spermic tubule, showing active spermatogenesis.

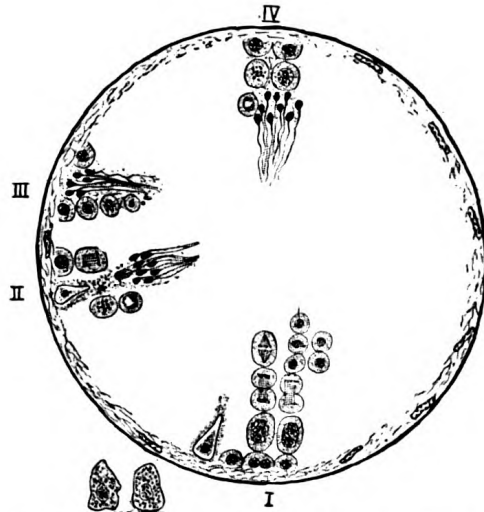


FIG. X.—*Diagram to illustrate Spermatogenesis.*
 I shows the various stages in the development of spermatozoa from spermatogenesis—spermatocytes—spermatids; II, the heads of the spermatozoa dipping into the cells of Sertoli; III, the further stage of development of spermatozoa; IV, mature spermatozoa with tails free in lumen prior to escape. Beneath are two interstitial cells.

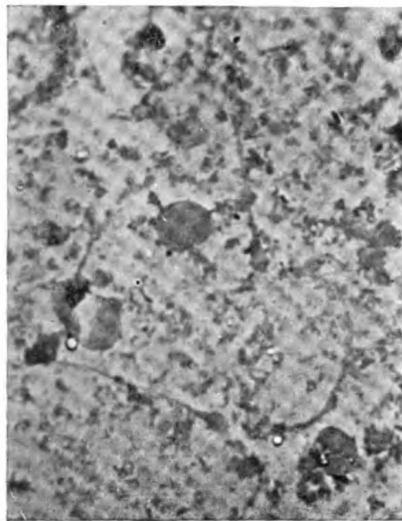


FIG. XI.—*Film of Fluid from Vesicula Seminalis of Case of Dementia Praecox Early Second Stage; died of Acute Lobar Pneumonia after three days' illness. (Mag. 875.)*

The film was stained with haematoxylin and eosin. Only a few spermatozoa seen, and these take the acid dye and are degenerated. Compare with Fig. XII.

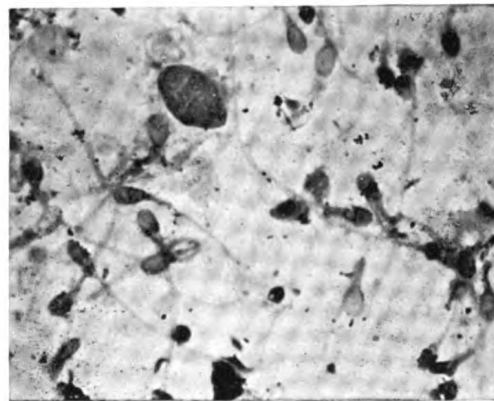


FIG. XII.—*Film of Fluid from Vesicula Seminalis of Case of Manic Depressive Insanity. (Mag. 875.)*
 The film was stained in a similar manner to Fig. XI. Observe that the spermatozoa are stained by the haematoxylin, and have a normal morphological appearance.

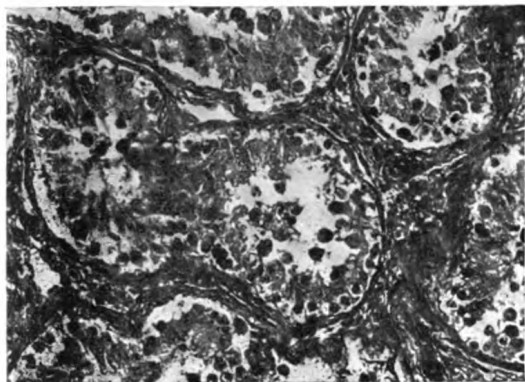


FIG. XIII.—*Testis from a Soldier dead from Sepsis caused by Bullet Wound of Lower End of Spinal Cord.* (Mag. 162.)
Spermatogenic tubules show no spermatozoa; most of the cells have undergone coagulation necrosis.

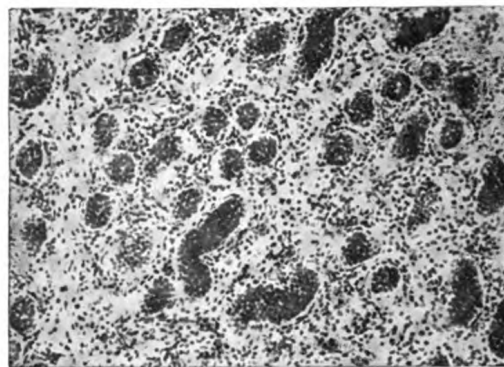


FIG. XIV.—*Testis from a Boy aged 7; dead of Chronic Tuberculosis.* (Mag. 105.)
The tubules are the same in size as at birth. Round-celled infiltration of interstitial tissue. No cells of Leydig seen. Compare with Fig. 1.

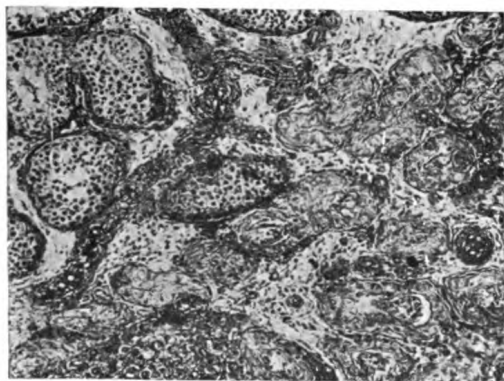


FIG. XV.—*Testis from a Case of General Paralysis.* (Mag. 96.)
To the left are normal seminiferous tubules. To the right are completely atrophied tubules. Below is a part of a nodule of interstitial cells.

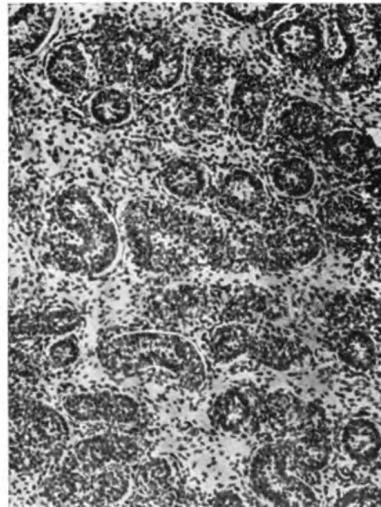


FIG. XVII.—*Testis of Juvenile Paralytic, symptoms of which commenced at the age of 8; death at 16.* (Mag. 105.)
The tubules are of the same size as those at birth. No cells of Leydig are seen in the interstitial tissue. Infantile interstitial tissue was well marked in this case. Compare with Figs. I and XIV.

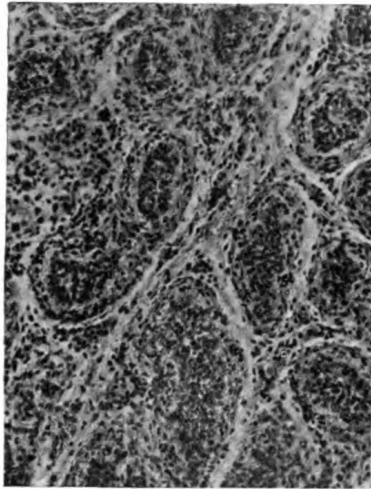


FIG. XVIII.—*Testis of Low Grade Imbecile with Congenital Epilepsy.* (Mag. 105.)

Basement membrane greatly thickened. The tubules contain only cells of Sertoli. No cells of Leydig seen in the interstitial tissue.

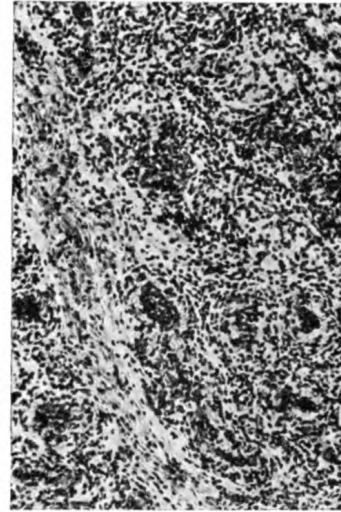


FIG. XIX.—*Testis of Idiot.*

The section is hardly recognizable as testis. The atrophied organs consist almost entirely of fibrous interstitial tissue. No Leydig cells seen.

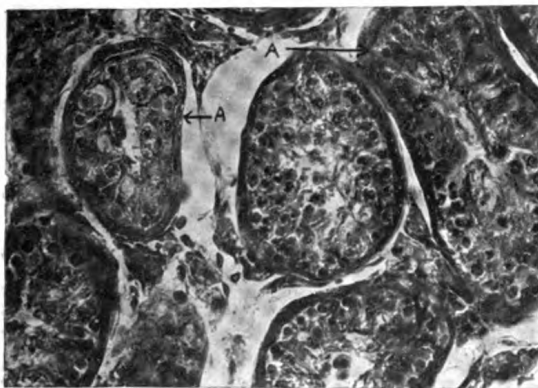


FIG. XX.—*Testis of Dementia Praecox Early Second Stage.* (Mag. 158.)

Atrophied tubules (A, A) showing thickened basement membrane lined mainly by empty cells of Sertoli. No spermatocytes seen in these tubules.

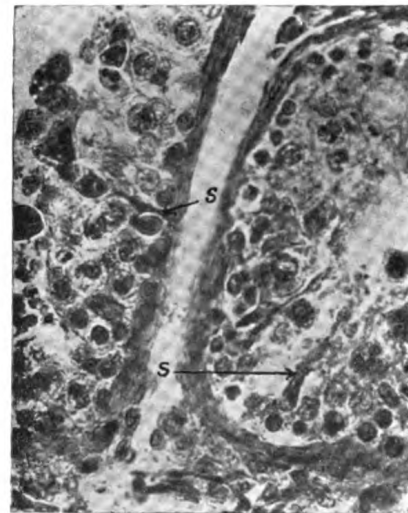


FIG. XXI.—*Testis of Dementia Praecox Early Second Stage.* (Mag. 394.)

The same showing (s, s) the empty cells of Sertoli. Observe the poor and unequal nuclear staining.

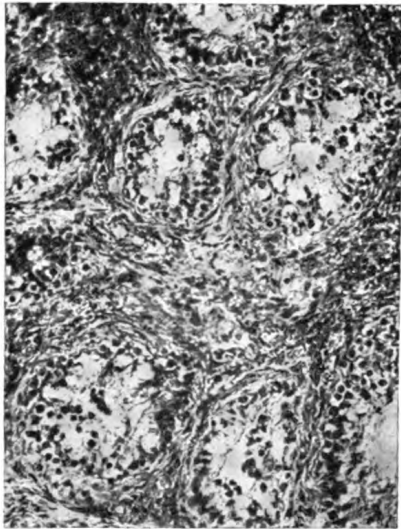


FIG. XXII.—*Testis of advanced Dementia Praecox in a Young Adolescent.*
(Mag. 162.)

Thickened basement membrane, increase of interstitial tissue. Complete arrest of spermatogenesis in all its stages. The contents of the tubules mainly Sertoli cells and sustentacular framework.

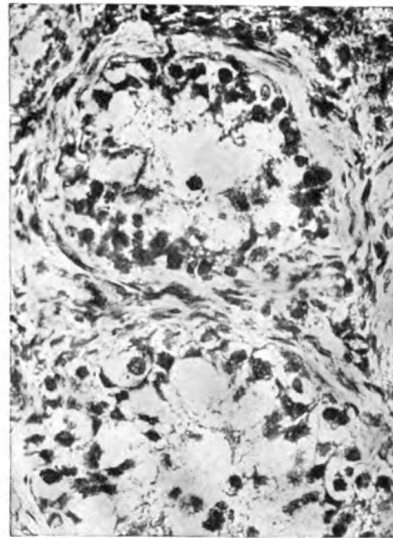


FIG. XXIII.—*Testis of advanced Dementia Praecox in a Young Adolescent.*
(Mag. 500.)

Two tubules of Fig. XXII more highly magnified.

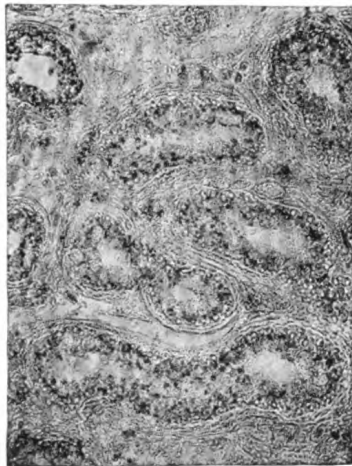


FIG. XXIV.—*Testis of advanced Dementia Praecox in a Young Adolescent.*
(Mag. 70.)

Scarlet-stained preparation for lipoid, very little interstitial lipoid. Black dots are lipoid and fatty acid in Sertoli cells.

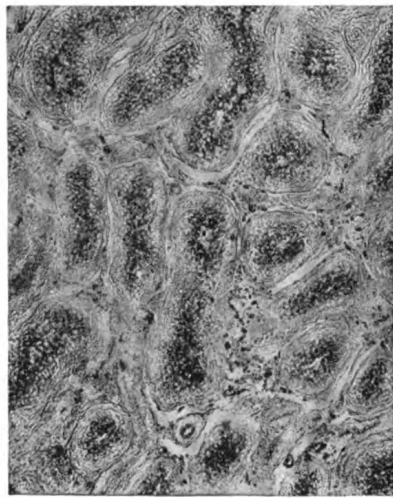


FIG. XXV.—*Testis of very advanced Dementia Praecox in a Young Adolescent.*
(Mag. 70.)

Scarlet-stained preparation for lipoids, very little interstitial lipoid, very thickened basement membrane. Fatty degenerated cells in tubules.

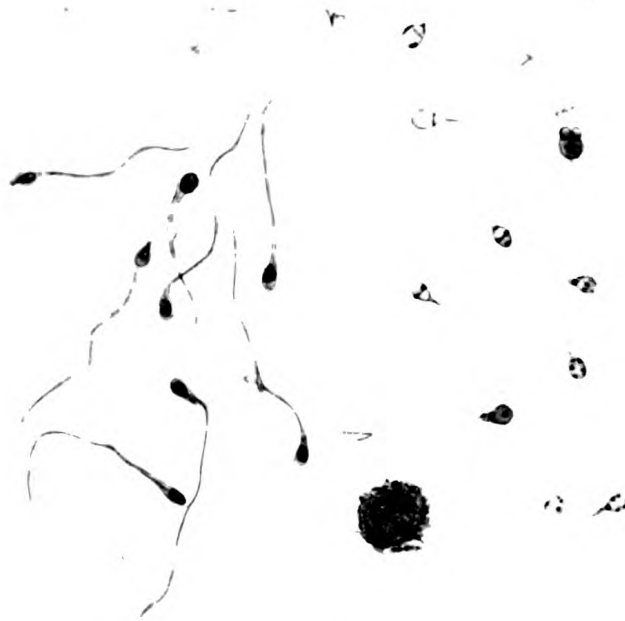


FIG. XXVII.

Normal spermatozoa from vesicula seminalis from a case of manic-depressive insanity; also degenerated spermatozoa from vesicula seminalis of a case of dementia praecox. Second stage. Haematoxylin-eosin. (Magnification 600.)

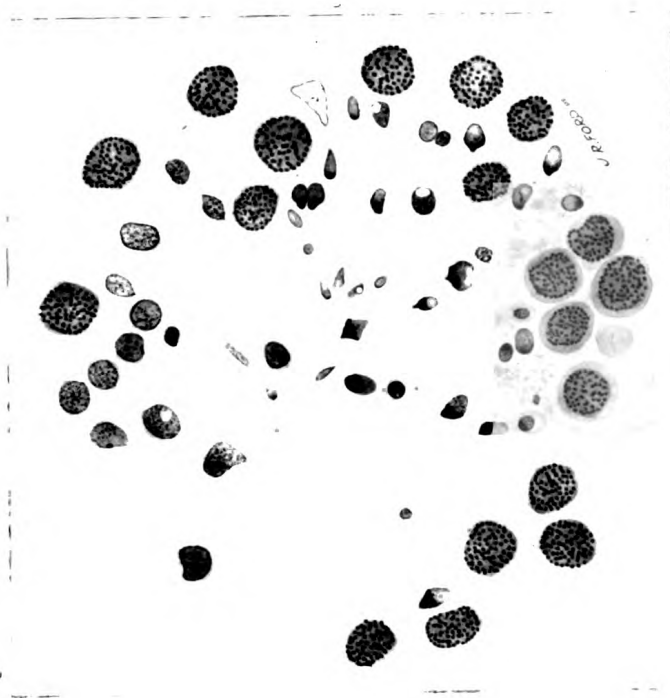


FIG. XXVI.

Section of seminiferous tubule stained by haematoxylin and eosin from the testicle of a case of dementia praecox of less than two years duration. The large nucleated cells are spermatocytes; the smaller bodies are spermatids or spermatozoa. Observe the varying size and shape, instead of being oval or of a lance head form. Some are vacuolated; others, especially the smaller, are stained entirely by the acid dye instead of the basic. There does not appear to be a normal spermatid or spermatozoa in this section of the tubule. (Magnification 400.)

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Section of Psychiatry.

President—Dr. WILLIAM McDougall, F.R.S.

Studies in the Pathology of Dementia Præcox.¹

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F.R.C.P.

INTRODUCTION.

For some years past I have been interested in the pathology of dementia præcox. First I investigated the reproductive organs, and I have already published in recent numbers of the *British Medical Journal* a paper on "The Investigation of the Testes in 100 Cases of Deaths in Hospitals and Asylums at all Ages from Birth to 80 Years and over." In this paper I have shown that in a large proportion of the cases of dementia præcox there is a complete arrest of spermatogenesis, and in all cases a more or less regressive atrophy is shown, the degree of change as a general rule depending upon the age at which the mental symptoms were first manifested and the time elapsing between the onset and death (*vide* Plate VI, figs. 1 and 2). In some cases in which the clinical history showed that mental symptoms had occurred in the prepuberal or puberal periods spermatogenesis may never have occurred. Now, in spermatogenesis we have a most active nuclear proliferation going on continually, and the histological evidence shows that the nucleic acid, which is the principal substance of the nuclear matter, is formed from a phosphorized lipoid contained especially in the cells of Sertoli.

The head of the spermatozoon consists of a protamin nucleinate and the tails, which are formed in these nurse cells of Sertoli, consist almost entirely of lecithin and cholesterol.

I will not go into further details on this point, but I should like to

¹ At a meeting of the Section, held November 11, 1919.

point out that where active spermatogenesis is going on there we find abundance of the lipoid granules; the same regions which show the existence of these lipoid granules also show the oxidase reaction; by this I mean that these granules play an important part in the chemical processes connected with the function of spermatogenesis. The oxygen on the surface of the lipoid granules is molecular oxygen, but in order to become nascent, chemically active oxygen, the molecule of O_2 must be converted into atomic oxygen, and this is effected by the catalytic action of the phosphorus and iron contained in the nuclei of the spermatogenic cells. A continual process of decomposition and recombination, in which oxygen plays an important part in building up the fresh nuclear matter, takes place.

Nucleic acid which forms the main constituent of the heads of the spermatozoa, as was shown by Miescher and Kossel's experiments, contains a large amount of organic phosphorus, iron and calcium. All nuclei contain these three important elements in addition to the elements of a proteid. The arrest of spermatogenesis may then be due either to a failure of one or more of these elements in the circulating blood or to an inherent biochemical lack of durability of the germ plasm.

The reason why I have given this short account of the failure of nuclear matter in the reproductive organs in dementia præcox (for it occurs in the ovaries as well as in the testes) is that the essential histological morbid change in the nervous elements of dementia præcox, as Nissl and Alzheimer pointed out long ago, is one of nuclear decay.

Nature is unmindful of the individual, mindful only of the species, for the body is but a vehicle for the germ plasm. During foetal life internal secretion of the sex determinant cells is active in establishing sex characters; after birth till puberty all the productive vital energy is concentrated on the somatic cells to build up a body capable of fulfilling nature's supreme biological end—reproduction. I have shown that the interstitial cells forming a well-marked gland in the testes at birth in a few months shrink and become quiescent functionally; the spermatogenic tubules at three months have grown to twice the size of those at birth and no further change takes place till puberty, when the interstitial cells reappear and are filled with lipoid substance and active spermatogenesis begins. Simultaneously with this concentration of productive energy on reproduction, the sexual internal secretion passes into the blood and produces the secondary sexual bodily characters: at the same time it effects a complete mental revolution. At first a vague ill-defined longing occurs, and this develops sooner or later into an all-prevailing desire

arousing new sentiments, passions, and behaviour, presenting many biological characteristics peculiar to each sex.

The critical periods of life as regards mental disease are adolescence and the climacteric periods of life when the sexual function matures and wanes. This affords *a priori* evidence of the important relation between the sexual functions and disease of the mind. This question naturally arises: Is the regressive atrophy of the reproductive organs the cause of the mental changes? (a) By its disturbing influence on the whole endocrine system of glands; (b) by the suppression of the normal sexual impulse, *libido*, of attraction to the opposite sex; (c) or is it a concomitant evidence of an inherent lack of vital energy germinal in origin? I incline to the last explanation as being the most probable although I consider the other two may in certain cases act as important contributing factors for the following reasons:—

(1) There is a general lowered vital reaction of the tissues of the body.

(2) The morbid changes are most marked in the cortex cerebri and primarily and especially affect the nuclei of the neurones.

(3) A number of the cases of dementia præcox show prepuberal clinical signs with history of arrest of development of mind which can be explained by the arrest and failure of development of cortical neurones: and at puberty when the stress of productive energy of the reproductive organs occurs nuclear neuronic decay sets in. This decay is probably owing to a germinal inborn lack of durability, for there is simultaneously a progressive failure of nuclear proliferation in the organs of reproduction.

At what period in early life this nuclear decay of the brain and of the reproductive organs begins it is difficult to say in individual cases; but I am of the opinion, from histological observations, that it may begin in some cases before puberty—even long before puberty. Kräpelin points to the fact that in many cases clinical symptoms occur in pre-puberal life, so that it is legitimate to conclude that there are a number of cases which might be termed dementia præcossissima.

Having given this brief introduction it is necessary now to lay down certain physiological and anatomical premises.

THE OXIDASE REACTION.

If a portion of brain or a section of spinal cord be stained for the oxidase reaction the grey matter is coloured blue, the white matter is unstained.

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Marinesco has demonstrated that histological examination of the sections shows that the cytoplasm of the ganglion cells, as well as their protoplasmic prolongations, are studded all over with fine blue-stained granules. Neither the nucleus nor the axis cylinder process contains any trace of granules. This agrees with the observations made by this author and myself in respect to the absence of refractile granules in the nucleus and axon when a living nerve cell is examined with the ultramicroscope. Marinesco found these granules in the cells of the choroid plexus but none in the neuroglia cells. Marinesco remarks it is probable that these oxidase granules belong to the neurone terminals which constitute the synapse and establish connexions between the different neurones.

"It is especially in the plexiform layers, as is the case for the so-called granule layer of the cerebellum and of the brain, that these oxidase granules are very numerous."

These facts clearly indicate that oxidation processes take place in the grey matter and that the intercalary cells, Type II Golgi (granules), which form the physiological link in systems of neurones of the first type, play an important part in the chemico-physical processes of the synapses.

Now, if oxidation processes which occur in the grey matter are essential for all nervous activity (including psychical), and if it be that molecular oxygen of the oxidase granules must be converted into free atomic oxygen, to ensure neuron function, it follows that deprivation of oxygen carried in the circulating blood will cause suspension of function. This is the case, for Mosso has shown, in a patient of his who had been trephined, that unconsciousness invariably occurred six seconds after pulsation in the brain had been caused to cease by compression of both carotid arteries.

It is calculated that there is six times as much blood in the grey matter as in the white matter. It was asserted by Leonard Hill that the oxygen content of the blood leaving the brain was as great as that of the blood entering. Bayliss gives reasons why this conclusion is not valid. Moreover, it must be remembered that the amount of grey matter to white matter in the brain is relatively small, and we know that no active oxidation processes take place in the white matter. This fact also disposes of the argument that Battelli's observations show that relatively to other organs in the body the peroxidase reaction of the brain is feeble.

It may be concluded therefore that oxidation processes are essential for neural function and that oxygen for cerebral activity is continually being used up and replenished by the blood. I have shown that there is no free oxygen in the cerebro-spinal fluid, but there is as much CO₂ free and combined as in the lymph. If the neurones are bathed by the cerebro-spinal fluid the sugar in the fluid may be a source of energy for the nervous system and be continuously undergoing a process of oxidation.

Now to continue the argument we may assume the following premises:—

All psychical processes are subordinate to physiological processes, that is neural activity.

All neural activity is dependent upon oxidation processes. These oxidation processes occur in the grey matter.

Oxidation processes are dependent upon the liberation of atomic oxygen from oxidase granules.

The oxidase granules are found on the body of the cell and the dendritic processes. They are especially abundant in the granule layers of the brain and the cerebellum. These granules are the intercalary neurones, second type of Golgi, and where they form definite layers they are interposed between radial fibres and the dendrites of neurones of the first type of Golgi forming a synapsis.

Granted Marinesco's observation, that in the granular layer the oxidase granules are especially abundant, it will be here especially that the atomic oxygen will be liberated under the influence of a catalase. Now the intercalary neurones have relatively only a small amount of cytoplasm compared to the size of the nucleus.

If the iron or phosphorus or both of the nucleus acts as a catalyser, as there is reason to believe, it may be hypothecated that when a stimulus arrives at the layer of intercalary neurones a catalase is liberated from the abundant nuclear substance; this acts upon the molecular oxygen attached to the oxidase granules, converting it into free atomic oxygen whereby physical and chemical changes occur, which either result in a physiological junction of the processes of the intercalary neurones by amœboid movement and multiple contacts with the processes of the first type of neurones, or a process of combustion occurs whereby the sugar is converted into energy which serves as a source of stimulus to the next system of neurones.

Whatever it be, it is significant that these intercalary neurones should exist in well-defined layers and in such abundance in cortical

situations where radiating and association tracts of fibres are ending—e.g., the calcarine region where there is a double layer of granules.

Again the great abundance of granules in the cerebellum is very significant for the following reasons:—

The cerebellum is an organ of uniform structure; it is present in all mammals. In fact, in fast swimming fishes and mammals, e.g., seals and sea-lions, it is very large; it is very large in all fast flying birds, especially birds of prey. This biological fact, together with the results of experiments on animals and clinico-anatomical observations in man, show that this portion of the brain is an organ of reinforcement of muscular action, and continuous tonic contraction of the muscles depends upon its functional activity. Under the influence of stimuli from the skin, especially the soles of the feet and all the structures of locomotion, the eyes and particularly the semicircular canals, a continuous discharge of neural energy along the rubro-spinal and vestibulo-spinal tracts takes place, reinforcing with varying degrees of intensity as required, the discharge from the spinal motor neurones to the muscles. It has been shown by Luciani that removal of the cerebellum in animals causes asthenia, astasia and ataxia. The layer of granules which form such a striking feature of the cerebellum may be assumed to provide an abundance of catalase for the conversion of the molecular oxygen into atomic oxygen and thus effect a continuous flow of neural energy. These and other considerations show that the oxidation processes necessary for neural activity take place at the junction of the intercalary neurones with the neurones of the first type. It is here that delay occurs in the transmission of a stimulus along a system of neurones. It may be assumed that either the chemical changes connected with oxidation are transformed into a physical stimulus which travels along the next neuron of the first type, or the oxidation processes cause either an alteration of the surface tension or an amoeboid movement whereby a physiological junction is effected at the synapse so that the original impulse can be transmitted. The extent, character, and intensity of the stimulus and its motor reaction are largely dependent upon the biological quality of the stimulus, for groups and systems of neurones are attuned by an instinctive memory or bio-rhythm to react to a biological stimulus with a specific rhythm with maximum intensity, but owing to the fact that a system of neurones with a special function is attuned to a specific biorhythm, a stimulus of any kind will give rise to a specific effect. This fact is proved by a simple experiment. A faradic current applied to the skin causes an uncomfortable vibration

sensation; applied to the tongue, a taste sensation; to the eyeball, a sensation of light; to the drum of the ear, an ill-defined auditory sensation. So that owing to this inherent specific bio-rhythm of the special sense neurones, the same stimulus produces the specific effect. It may be presumed that a common mode of motion has been transformed to a special mode of motion at the central receptor.

Oxidation processes do not take place in nerve, and it is incapable of fatigue. The nervous impulse as it travels along the axon is a physical disturbance unattended with any chemical change, but when the impulse reaches the terminal brush of fibrils in the grey matter it liberates a catalase and oxidation processes occur.

NISSL GRANULES, AN ARTEFACT, BUT THEIR PRESENCE OR ABSENCE IN DEAD CELLS OF GREAT SIGNIFICANCE.

The living nerve cell does not contain Nissl granules but a number of minute oval or spherical granules, which, if they escape from the cell remain discrete. By dark ground illumination they reflect the light and appear white, by direct illumination they appear dark and very much like an emulsion. When the cell dies these disappear, and if certain fixing reagents, such as alcohol, formol, or sublimate solution be employed, a coagulation of the proteid constituents of the cytoplasm occurs causing the formation of the Nissl granules. These granules, as shown by their staining reaction with basic dye, consist of a basophil substance.

Significance of the disappearance of Nissl Granules.

The cytoplasm of all nerve cells contains this basophil substance, and inasmuch as it diminishes in amount or even disappears in exhausted cells it has been supposed to be the energy substance of the cell—hence has been termed kinetoplasm. Consequently, although the basophil substance does not exist in the form of Nissl granules in the living cells, yet a comparison of the histological appearances, as to its distribution and amount in normal cells, with the appearances presented by similar cells in morbid conditions, affords a reliable method of determining functional or organic changes of the neurones.

The Nissl granules are especially abundant and form a tigroid pattern in the large motor and sensory cells of the stem of the brain and the spinal cord; they also exist in the Purkinje cells, the large pyramids of the cortex, and especially are they well seen in the Betz

cells. In the smaller cells they are not distinctly seen, but their cytoplasm contains basophil substance in all normal cells of Golgi type I.

Morphological changes in the cytoplasm as regards the amount, distribution, and arrangement of the basophil substance (chromatolysis), may therefore be correlated with disease and functional disorders of particular systems and communities of neurones having specialized functions.

Still more important are biochemical changes indicated by an alteration in the staining reactions of the cell, for they may point to a morbid state or to the death of the cell. Whereas the morphological change previously referred to leads to depression or *suspension* of function—a biochemical change indicates a *suppression* of function. If polychrome or toluidin blue and eosin dyes be employed for staining sections we may obtain a basophil and acidophil reaction; thus a motor cell which is dead, e.g., from experimental anæmia or hyperpyrexia, stains a diffuse dull purple, the processes as well as the body of the cell having a homogeneous instead of a differential reaction to the dyes.

Macallum has shown that the Nissl granules contain both iron and phosphorus; the basophil substance is therefore a nucleo-proteid and, as I pointed out in my Croonian Lectures in 1900, diminution of this substance may be “an expression of the diminution of the vital interaction of the highly phosphorized nucleus upon the cytoplasm.”

The abundance of nucleo-proteid, with its important iron, calcium and phosphorus constituents in the cytoplasm of the large multipolar motor cells, may be correlated with a greater chemico-physical change in large cells with large and relatively long axons.

The small intercalary neurones (second type of Golgi) have little or no basophil substance in the cytoplasm; the nucleus is relatively very large, but we have seen that these cells enter into the synapse of neurones of the first type.

LIPOID GRANULES IN THE CELL AND THEIR SIGNIFICANCE.

In healthy young animals lipid granules are not seen in the cytoplasm of the neurones; they are found in the cells of old animals. These granules are also found in varying amount in the cells of the brain and spinal cord of human beings dying of various diseases. Thus I have found them in abundance in myasthenia gravis, in death from shock caused by compound comminuted fracture of the thigh from

gunshot wound. They are found in old people dying of various diseases, but I have found them especially abundant in dementia senilis, general paralysis, dementia præcox, and amaurotic idiocy.

Pighini has made a special study of the cause of their appearance, and has shown that if pieces of the brain of a healthy dog are kept in Locke's fluid in a warm chamber for twenty-four hours, these granules appear and increase in number with the length of time the tissue is kept under these conditions. Controls showed that these were not present in the tissue before they were placed under these conditions.

The facts seem to show that up to a certain point the presence of these lipid granules may be within physiological limits and be only a sign of deficient metabolism, incidental to a failure of complete oxidation processes; and their existence therefore is not inconsistent with a normal, although probably lowered, functional activity of the neurones so affected. But when the cytoplasm of a large number of cells contains abundance of these granules the physiological limit has been passed and they are an indication of a pathological condition associated with a depression of function sufficient to give rise to impairment or even cessation of function. In amaurotic idiocy the whole of the neurones throughout the cell body are filled with scarlet stained globules. In dementia præcox the cells of the cortex, the basal ganglia, and the medulla exhibit this change. Especially does the process affect the cells of the frontal lobes (*vide* Plate I). Pighini concludes that these fat granules are unsaturated phosphatides for they yield a blue-violet colour with Nile blue sulphate.

These granules stain red with Sudan III, and according to Pighini this would indicate a participation of cholesterin or of its esters with cerebroside. The tendency of the granules to stain a violet-blue colour with Nile blue also suggests the presence of cholesterin. He believes that Marinesco and Obersteiner were correct in considering that these lipid granules in the nerve cells of old people are products of regressive metabolism, and that hypo-oxidation and pathological processes in which katabolism exceeded anabolism would account for their occurrence—they are probably therefore an expression of anabolic hypofunction.

Having thus considered in detail certain anatomical and physiological facts concerning normal neural structure and function we are prepared to estimate the significance of the morbid changes observed in dementia præcox and see how far they could account for the fundamental disorders of the mind in this disease. I will commence the subject with a brief reference to the supposed causes.

CAUSES OF DEMENTIA PRÆCOX.

With regard to the cause of dementia præcox Kräpelin states that, in the absence of recognizable external causes, it is possible only to think of auto-intoxication which may have some remote connexion with the sexual organs. Kräpelin has pointed to the fact that in a number of cases of dementia præcox the degenerative process began before puberty. He states:—

“The conclusion seems to me justified that the psychic abnormalities which precede the real onset of dementia præcox already represent, in fact at least, the action of the cause of the disease, even if they can be traced back into the first years of the patient's life. The commencement of the malady would be, if this view should be confirmed, moved back into childhood, for a considerable number of the patients we should have to assume a longer or shorter preparatory stage, in which without noticeable progress, but already in indications, the disease develops certain results such as we find again most strongly marked at the height of its development and in the terminal phases. This interpretation finds essential support ‘as it appears to me’ in the dementia præcox of children and in engrafted hebephrenia.”

My observations show that the appearances of the testes in those early cases of dementia præcox, in which there is a complete abolition of any sign of spermatogenesis, would rather lend support to the view that the regressive atrophy may have commenced before puberty in some cases. For I have observed that in some cases even after months or even several years of mental symptoms pointing to dementia præcox, and, in the notes of which, in not a few, excessive masturbation has been recorded, there exists with the signs of regressive atrophy in many of the tubules still evidence in other tubules of active spermatogenesis. So also in some females the ovaries show Graafian follicles and corpora lutea together with atretic follicles and degenerated ova. Kräpelin asserts that 14 per cent. to 15 per cent. of all inmates of the asylums suffer with this form of mental disease. He dismisses the idea that masturbation is the cause, for reasons which are apparent, viz., masturbation occurs in other mental diseases. Dementia præcox is as common in women as in men and therefore the loss of seminal fluid by the latter, as a result of masturbation, cannot be the cause.

Kräpelin accepts Bleuler's distinction of *fundamental disorders* and *accompanying phenomena* of the disease. *The fundamental disorders* are those which occur in dementia simplex and in the terminal state of *simple weak-mindedness*. From this point of view the weakening

of judgment, attention, of mental activity and of creative ability, the dulling of emotional interest, and the loss of energy, lastly the loosening of the inner unity of the psychic life would constitute the fundamental disorders while all the remaining morbid symptoms, especially hallucinations and delusions but also the state of excitement, depression and stupor, further the manifold disorders of volition, negativism, automatism, stereotypy, automatic obedience, mannerisms, grimacing, outbursts of meaningless laughter, &c., would be regarded as secondary *accompanying phenomena* due to disruption of harmonious psychic interconnexions by the degenerative process affecting functional systems of neurones in varying degrees of severity.

The fact that primary dementia of adolescence occurs in uncivilized races as well as civilized, supports the notion that this disease is of endogenous origin. The nature of the accompanying phenomena probably largely depends upon the evolution of the individual psychic personality ; and in this connexion it is interesting to note that Kräpelin found that auditory hallucinations were rare among the native Javanese. Doubtless word symbols play an unimportant part in their mentality as compared with civilized Europeans.

HISTOLOGICAL MORBID CHANGES IN DEMENTIA PRÆCOX AS DESCRIBED BY VARIOUS AUTHORS.

Histological investigations hitherto, with the exception of the examination in a few isolated cases of the sexual organs, have been devoted to the central nervous system, especially the cerebral cortex.

Macroscopically, the brain and the spinal cord in these cases show little evidence of any disease.

Microscopic investigations by numerous neuro-pathologists, notably Nissl, Alzheimer, Duston, and workers (Rae Gibson and Harper Smith) in my own laboratory, have arrived, broadly speaking, at similar results.

Kräpelin sums up the changes thus :—

“ Nissl, in the cases of chronic evolution, has noted profound modification of the cells which he has described under the name ‘Destruction of the Nucleus.’ A considerable number of cells appeared to be destroyed but there is no atrophy of the cortex. The deep layers contain numerous and large neuroglial cells.”

Alzheimer, studying histological lesions in acute cases of catatonia, has described grave alterations of the cells of the cortex, especially of the deeper layers, notably swelling of the nuclei, infolding of their

membrane, the cellular body retracted and on the way to destruction, and neoformation of neuroglial fibrils which surround the cells.

In the old chronic cases, Alzheimer found widespread changes in the cells which may be regarded as the terminal state of grave disease which has run its course, in particular sclerotic forms. Very frequently deposits of lipoid products of decomposition were found in the various cells, even in quite young persons. Strikingly frequent were groups of nerve cells in which the basal processes appeared to be swollen and deformed by accumulation of fat. Lastly, diffuse loss of cortical cells could be observed. These severe morbid changes affected especially the second and third cortical layers.

The observations of Klippel and L'Hermitte have shown that these primary degenerative changes of the neurones may affect the whole central nervous system; and they consider that they are either due to an inborn biochemical deficiency or to the effects of an autotoxin circulating in the blood after the reproductive organs have arrived or should have arrived at maturity.

Klippel and L'Hermitte have estimated volumetrically the number of cells affected in different parts of the cortex. Their conclusions are of importance and may be thus summarized:—

(1) The lesions rarely affect the vessels of the brain and spinal cord, and only in restricted points the neuroglia, and there exists neither diapedesis nor lesions of the endothelial walls of the vessels nor of the connective tissue cells.

(2) The lesions of the neurones can be divided into three categories corresponding to the chronological order of their development.

(a) Pre-existing lesions, not constant and of congenital origin, constituted by anomalies of development.

(b) The lesions of the neurones developed at the same time and in the course of the disease, and consist in atrophy of the neurone with early granulo-pigmentary degeneration.

(c) Consecutive lesions marked by arrest of growth affecting the neurone, but also in different degrees the whole organism.

Whereas diffuse lesions are localized in the centres of association, the integrity of the constituent groups of the projection systems of the neurones was in general preserved.

Klippel and L'Hermitte have since called attention to the lesions of the spinal cord in dementia præcox, in particular to degenerative lesions of the posterior column.

Wada states that he has found the large pyramidal cells are comparatively less affected.

Sioli remarks upon the accumulation of lipoid disintegrated material in the tissues especially around the vessels. Most authorities make little mention of extensive fibril destruction, although some authors note changes, and Goldstein asserts that in particular the coarser fibrils are damaged. De Buck, and others, refer to attenuation of the fibres in the supraradial network.

All investigators refer to glia cell proliferation. Alzheimer, in acute cases, describes amœboid hyperplasia of neuroglia, accumulation of glia cells round the nerve cells and morbid new formation of fibres which surround the cells in a particular manner. Nearly all authors refer to the large swollen pale nuclei of the glia cells, many of which can be seen adherent to, or even penetrating into, the decaying nerve cells.

None of the authors refer to the change in the granule layers.

The histological investigations of the central nervous system in dementia præcox of all these eminent authorities are in agreement on certain fundamental points, viz., that there is a parenchymatous degeneration of the neurones, and that the affection of the mesodermic vascular and supporting tissues are slight and of little importance; contrasting therefore most distinctly with the meningo-encephalitis of dementia paralytica and sleeping sickness, both of which are due to a parasitic infection of the central nervous system.

The results of these observers clearly point to a primary parenchymatous degenerative process of the neurones and are in favour of the unicist conception of Kräpelin.

SUMMARY OF PERSONAL HISTOLOGICAL OBSERVATIONS.

None of the eight cases examined showed any thickening of membranes or obvious naked-eye change of the brain; in that respect contrasting plainly with dementia paralytica. Five of the cases died in pre-war times. Paraffin block sections of various portions of the brains were prepared of 5 μ or 10 μ in thickness, stained by polychrome methylene blue or methylene blue and eosin. The remaining three were cases that have died within the last year or two. In these the brain was systematically examined both by paraffin block sections, stained in the same way as above, and frozen sections of formol-hardened material stained with scharlach and Nile blue for lipoid granules.

The sections which had been prepared in pre-war days had retained their colour, and the results of the histological examina-

tion of these sections appended to the clinical notes of each conform, so far as they go, with the results obtained in the recent cases.

Broadly speaking, the morphological changes correspond with those described by the previously mentioned authorities. They confirm the results obtained by Klippel and L'Hermitte regarding the extension of the degenerative cell changes to the whole brain, including in two cases the cerebellum. They also show that there are two types: (1) In which there has been a congenital arrest of many neurones, especially of the small and medium sized pyramids in the frontal lobe (amentia, admirably described many years ago by Shaw Bolton) and in which later at puberty or adolescence, a widespread neuronic degeneration occurs. (2) The degenerative cell process is not associated with any congenital or prepuberal arrest of development.

The glia cell proliferation is general, and occurs especially in regions where the cell degenerative process is most marked. The neuroglia nuclei are pale in colour, and seen in groups around the degenerated cells, sticking to them or penetrating the cytoplasm. I could see no spider cells, and only slight evidence of neuroglia fibril formation by Ranke's Victorian blue stain, so characteristic of general paralysis.

The vessels show no changes: there is no perivascular cell infiltration, nor endothelial proliferation of the capillaries, so characteristic of the meningo-encephalitis of dementia paralytica. Around the small vessels and in the endothelial cells, especially of the frontal lobe, fatty lipid granules are found (*see* Plate I).

There is little evidence of nerve-fibre atrophy and sections of the brain stained by the Weigert-Pal method would afford but little explanation of the dementia. Such fibre atrophy or deficiency as occurs could be explained by the destructive decay of the cortical cells, or the congenital cell deficiency. The fibre deficiency or atrophy is most apparent in the frontal lobes.

But the amount of fibre atrophy, due to cell destruction in those cases in which the demential symptoms came on first at puberty or in early adolescence, does not show a correspondence as in dementia paralytica. That being the case, we must assign the major part of the fundamental symptoms of dementia præcox to the functionally incapacitated or degenerated neurones. By this I mean the greater part of the neurones are living, but so biochemically altered that a progressive disorder and loss of function results.

My observations show that, besides the morphological changes in the cells affecting the nucleus and the cytoplasm of the cells, which have

been described as occurring in the cortex by all the before mentioned authors, there are, in addition, similar, though not as intense, morphological changes in the basal ganglia, the stem of the brain, the medulla oblongata, and in severe cases of the cerebellum, but the cortical cells are most affected.

No author has paid attention, so far as I can find, to the marked nuclear and cytoplasmic changes in the layers of granules (intercalary neurones) of those regions of the cortex where these cells are so aggregated that they can easily be differentiated from the scattered pale nuclei of the neuroglia cells.

The swelling of the nucleus and infolding of the membrane of great numbers of the cells in the cortex, and to a less degree in the other regions of the brain mentioned, is well established, but no author has pointed out that numbers of the nuclei of these cells show, in varying degrees of intensity, a biochemical change by the fact that the nucleoli, which in normal cells are stained a deep blue (basi-chromatin) reaction, are stained purple or even reddish-pink (oxychromatin reaction). According to Heidenhain this oxychromatin colour with eosin and blue dyes signifies a diminution of organic phosphorus (*see* Plates). This diminution of organic phosphorus may be associated with diminished function in relation to oxidation processes.

Besides the biochemical and morphological changes of the nucleus, there are morphological and biochemical changes observable in the cytoplasm and its processes. Under a low-power magnification the cortical cells, especially the small and medium-sized pyramids, are seen to have their processes broken off, and the regular linear arrangement into the columns of Meynert may be more or less destroyed according to the advance of the disease.

There may in some cases, owing to congenital deficiency, be small places where the cells are absent. Examined with an oil immersion, normal Nissl granules are seldom seen, even in the large Betz cells or cells of the optic thalamus, corpus striatum, pons and medulla oblongata, but they are seen fairly normal in the anterior horns of the spinal cord.

Generally speaking, the Nissl pattern is not seen in the cells and dendrons, but the cytoplasm and processes are stained a dull diffuse bluish-purple, and scattered throughout are vacuoles.¹ These vacuoles are caused by lipid granules, which have been dissolved out in the

¹ Since writing this paper I have examined the inferior cervical ganglion, together with the structures named, from a recent fatal case of dementia præcox. The cells of the sympathetic ganglion showed abundant lipid granules so that it is probable that this change may be more or less universal in well marked cases of this disease.

process of preparation of the sections (*see* Plates III and V). As can be seen, frozen sections stained by scharlach or Nile blue show the cytoplasm more or less filled with fat granules (*see* Plate I). I have already given reasons for supposing that the basophil substance, which is the antecedent of the Nissl granules, is a product of the vital action of the nucleus on the cytoplasm, and the lipoid granules are evidence of hypofunction, which, when it is abundant and affecting many cells, may be regarded as a pathological process. So that the cells in all the regions mentioned, in all the cases more or less, exhibit direct evidence of hypofunction.

No author hitherto has directly investigated the condition of the intercalary cells, although reasons have been given for supposing that they play an important part in the formation of the synapse in all systems of neurones and in the cerebellum. Microscopic examination with an oil immersion of regions of the cortex in which these cells form definite layers visible with a very low magnification—e.g., the ascending parietal or occipital convolutions in the region of the line of Gennari and other areas, shows that these cells are profoundly modified. The nucleus is swollen with pale blue or purple staining, and often pink—indications of a biochemical change. The cytoplasm is hardly visible in these stellate neurones of the plexiform¹ layer (granular) owing to the swelling of the nucleus; fine vacuoles are, however, seen in it, and when these cells are stained for lipoid, fine orange-coloured granules are observed corresponding to the vacuoles.

Similarly in these cells this reaction constitutes evidence of a hypofunction and deficient oxidation. Having this in mind, I felt it would be desirable to see if this failing of the basophil substance could be demonstrable to the naked eye. I took, therefore, three pieces of tissue from three separate brains that had been hardened in formol. I selected the cerebellum because its structure is uniform, and therefore comparisons would be more reliable.

Portions of the cortex of the lateral lobe of a case of tetanus, a case of senile dementia, which showed by the usual staining methods marked changes similar but more extensive than dementia præcox, and a case of dementia præcox were taken. These were washed free of formalin and simultaneously passed through the various processes for blocking in paraffin. The three pieces in one block were cut simultaneously, the sections containing the three tissues were placed on cover glasses stained and mounted; so that the conditions in no way varied

¹ The term used by Cajal and Campbell for the granule layer.

for each section. The results are shown in the accompanying Plate II. It will be seen how much deeper blue the granules of the tetanus case are stained than are the sections of the brains of the two cases of dementia.

This observation, in conjunction with the previous microscopic observations, points to a deficiency of basophil substance and a diminution of the organic phosphorus in the cells of the brain of dementia præcox; a fact which may be correlated with the evidence of a failure of nuclear phosphorus in the reproductive organs. Further observations by chemical analysis of the cerebellum in dementia præcox and normal are in progress. But the following chemical investigations, although by no means conclusive, tend to support the microscopical investigations :—

CHEMICAL QUANTITATIVE ANALYSIS.

Waldemar Koch and Sydney Mann, in my laboratory, made a number of careful analyses of the brains of persons dying of different diseases, including six from cases of dementia præcox :—

“Compared with the normal, the amount and distribution of phosphorus shows no marked change, but the neutral sulphur shows a great diminution, while the inorganic and protein sulphur is greatly increased. Thus so far nine cases in all have been examined and found to give results which, although varying among themselves, all tend in the same direction—i.e., a *diminution of the neutral sulphur*.¹ This variation appears to be independent of the cause of death, and so far has not been found in other forms of insanity. It does not then seem unreasonable to suppose that the subject of this mental disorder may possibly possess a *general bodily deficiency* for oxidation processes. Some support is lent to this by the fact that Pighini has found an increase of neutral sulphur in the urine in this disease.”

These experiments are valuable inasmuch as they indicate deficient oxidation processes. The fact that these observers were unable to detect any diminution of organic phosphorus is easily explicable and in no way contradicts the micro-chemical staining reactions indicative of a deficiency of nucleic acid phosphorus. The reasons I would adduce are these :—

¹ An explanation may not be out of place for the term “neutral sulphur.” It represents an intermediary stage between unoxidized protein sulphur and oxidized ethereal and inorganic sulphates. It does not split off sulphuric acid on prolonged boiling with hydrochloric acid, neither does it form lead sulphide on boiling with alkali and lead acetate. The term *neutral* is used in contradistinction to sulphates or sulphuric acid.

(1) Not more than 2 per cent. of the brain consists of cells in the grey matter, and only a fraction of this consists of nuclear matter.

(2) The great bulk of the brain is white matter, and of this myelin, which contains a large amount of organic phosphorus is the largest constituent.

(3) There is no appreciable change in the myelin in dementia præcox; consequently, although the nuclear phosphorus may have diminished considerably in amount, it would be only a small, almost inappreciable amount of the total organic phosphorus in the brain.

Pighini has carefully studied metabolism in dementia præcox. He gives the following summary of his results:—

“ With a view of throwing light on the metabolic change associated with the profound symptoms of dementia præcox, I have selected four typical cases of the disease in the acute and eight in the more advanced stage, and in them I have studied the various food elements by means of numerous analyses of the food administered and the excretions. Each case gave results of interest, which may be summarized as follows:—

(1) In the dementia præcox of Kräpelin the acute phase and the advanced phase each present different modifications of altered metabolism.

(2) In the acute phase, as evidenced by motor restlessness, sitophobia, violent impulsiveness, slight elevation of temperature, &c., *there is a negative balance (increased excretion) of nitrogen (urea, uric acid xanthin bases) of phosphorus and sulphur, indicative of a marked dissolution of the phosphorized and sulphurized proteids of the organism.*

(3) In the advanced phase, as evinced by dementia, negativism, tics, grimaces, katatonia, &c., there is a proportionate retention of phosphorus and nitrogen, a loss of sulphur proportionate to these elements, and an independent loss of calcium.

(4) In the two phases investigated there is an altered water metabolism, and a relaxed excretion of chlorine.”

The great difficulties attending chemical analyses of the brain and the many sources of error in estimating metabolism in this class of patients makes one careful in drawing conclusions. Still such evidence as exists supports the view that there is a deficiency in the oxidation processes in the brain. Seeing that the microscopic investigations related tend to prove that the oxidation processes are deficient, these findings support the general premises deduced.

THE CORRELATION OF THE MORPHOLOGICAL MICRO-CHEMICAL AND
CHEMICAL INVESTIGATION OF THE BRAIN AND REPRODUCTIVE
ORGANS WITH THE FUNDAMENTAL CLINICAL SYMPTOMS.

A certain number of cases of dementia præcox occur in congenital aments, or imbeciles. These might be termed dementia præcossissima and from early childhood there are clinical indications of a failure of the higher neural functions. It is quite probable that not only the brain is affected by a developmental deficiency, but that there is a general deficiency of the *élan vitale* and this is manifested by the reproductive organs at puberty, which either fail to develop or an early arrest of spermatogenesis occurs. In this connexion it is interesting to note that I have shown a complete arrest of development of spermatogenesis in several cases of imbecility.

Cases in which clinical symptoms first manifest themselves at puberty or early adolescence exhibit a progressive failure of the *élan vitale*, which may be correlated with the regressive atrophy of the testes, organs in which it can be easily demonstrated that productive energy is most active. But the active nuclear proliferation continually going on in the testes is a synthetic process requiring active oxidation processes to build up a complex organic phosphorus compound, protamin nucleinate out of simple phosphorized lipid substances. The fact that these synthetic processes rapidly fail points to a germinal defect.

The *élan vitale* so poetically described by Shakespeare in "Romeo and Juliet" :—

" My bosom's lord sits lightly on his throne
And all day long an *unaccustomed spirit*
Lifts me above the ground with cheerful thoughts."

is a sign of an outburst of productive energy connected with the supreme function of reproduction.

There is also evidence of germinal defect, for many cases of dementia præcox are congenital aments as shown by the fact that a number of the higher cortical neurones do not develop.

The fundamental clinical disorders of dementia præcox are a weakening of judgment, attention, of mental activity and of creative ability, the dulling of emotional interest and the loss of energy, lastly the loosening of the inner unity of the psychic life. Now if we assume that the neuron changes show (1) a progressive *suspension* of function of some neurones associated with (2) such intense bio-chemical and

morphological changes in other neurones as to indicate suppression of function we are able to explain remission or partial remission of some of the symptoms, and sudden changes from stupor to impulsive behaviour.

Suspension of neuronic function due to hypofunction from defective oxidation processes caused by auto- or hetero-toxic conditions may vary in intensity and degree, but *suppression* of function owing to germinal lack of durability is incapable of any remission but is progressive, so that even when a remission of some of the symptoms occurs there is a residuum of weak-mindedness, *dementia simplex*, which is progressive and continuous. It should be mentioned that the neurones are in the normal individual permanent cells adapted for a prolonged life and protected by special anatomical conditions from injury and disease. Any form of stress, using the term in the wide sense employed by Mercier, will contribute to lower the durability of the neurones.

Now it is known that some cases which at first clinically appear to be cases of dementia præcox recover. Moreover, some cases of confusional insanity may present a clinical picture of dementia præcox and recover completely. It must be supposed that these cases are due to a hypofunction, and we should probably find a general condition of lipoid granules in the neurones with basophil chromatolysis and disappearance, or partial disappearance of the Nissl granules.

But evidence of a biochemical and morphological degeneration of the nucleus points to a condition which would end in suppression of function, although this condition does not necessarily imply death of the neurone and atrophy of the axon. The morphological changes implying *suppression* of function are found especially in the cortex and particularly the cortex of the frontal lobe in which neuroglia proliferation is most marked. Associated with this are universal changes in the various regions of the brain pointing to hypofunction, viz., lipoid granules in the cytoplasm and in many cells an oxychromatin or a tendency to an oxychromatin reaction of the nucleus (*see* Plates III and V).

The affection of the stellate intercalary cells which enter into the synapse, and the evidence I have adduced of the importance of these cells in connexion with oxidation processes productive of neural energy and transmission of nervous impulses, suggest that a hypofunction or suspension of function of these neurones would lead to synaptic dissociation and thereby account for psychic dissociation and the coming and going of symptoms; or where there is a permanent morbid change, to a suppression of their function with permanent dissociation.

We have thus two morphological conditions which will account for the fundamental disorders, and the nature of these disorders will depend upon the cerebral structures affected whether in such a way as to produce suppression or suspension of function. Naturally the nature of the mental disorders will also depend upon the localization and the relative intensity of the hypofunction, suspension, or suppression of function of the neurones.

It is quite probable that there is a hypofunction of the whole of the bodily tissues; there is certainly a diminished vital resistance to microbial infections. A large percentage of these cases of dementia præcox die of tuberculosis, but my observations show that exactly the same neuronic changes can be found in dementia præcox cases that have died of acute pneumonia. So that although it is common to find stupor in patients affected with active tuberculosis and although the absorption of toxins may, therefore, have played a part in the production of some of the symptoms, yet I have formed the conclusion that the essential cause of this disease is an inborn germinal defect, the nature of which is unknown. When we come to consider that in a normal seminal emission there are about 226,000,000 spermatozoa, it is probable that some are of greater vitality than others, and that by the law of chance a weak spermatozoon may occasionally reach the ovum, or the ovum itself may be deficient in vital energy. Again the combination may not be favourable to the production of a sound and durable organism. That this chance of a spermatozoon being vitally deficient would be increased by hereditary taint, or by any of the causes which would lower the vitality of the parents, seems probable.

Nature is unmindful of the individual, mindful only of the species, and by early mental decay and arrest of spermatogenesis, reproduction of a degenerate being is thereby prevented.

CASE I.—DEMENTIA PRÆCOX.

W. H. *Previous History*.—According to the statements of the patient he joined, as a boy, the Somerset Light Infantry in November, 1912, and was in the band. After two years and fifty-six days' service he was discharged for deafness. He rejoined the Army in March, 1915, and was sent to France. Whilst at Dickabush in November, 1915, a shell burst near him and he was sent to the base, suffering from shell shock. From there he was sent to Faversham, Chatham, and Mill Hill, and finally discharged as unfit for further service. After leaving the Army he apparently did no good. He had many jobs, but admitted he could not keep them, and had been in prison for being in possession

of matches whilst on munition work. He was admitted to Long Grove Mental Hospital on June 3, 1918, aged 20.

Condition on Admission.—*Physical condition:* Good; comparatively normal and of average development.

Mental Condition.—He was found to be suffering from recent melancholia and was an evident case of dementia præcox. He had several mannerisms and laughed and grinned inanely, was full of all sorts of strange fantasies and ideas and said he felt he was under some influence or spell. He was very solitary and uninterested in anything except his own peculiar ideas. He himself thought he had always been strange, even before joining the Army, but that he had been much worse since sustaining shell shock. He was evidently hallucinated and sometimes very confused and contradictory. He accounts for his fits of depression in a very inconsequential way, and even when saying that he had asked the attendants at the infirmary to poison him he began to smile in an imbecile way.

In July, 1918, his mental condition was deluded and hallucinated, restless, impulsive and resistive, with occasional faulty habits. On one occasion he butted his head against the wall and at another time he threw himself about the floor. This condition continued with lapses into a mildly stuporose condition.

On October 12 he threw a flower pot at an attendant, and on November 1 he was noted as being in an unsettled condition, aggressive, impulsive and intolerant of discipline.

On November 11, 1918, he was transferred to Hanwell Mental Hospital where he was diagnosed as dementia præcox, his mental condition being one of moroseness and confusion, refusing to speak, but with outbursts of aggressiveness and violence.

On December 6, 1918, he was noted as showing no improvement in his mental condition, but his physical condition was good and he was clean in his habits.

Throughout the later part of January and February, 1919, he was troubled with a low form of pneumonia and a persistent cough. This condition however cleared up and his health was good. His mental condition showed no improvement and he continued to be dangerously impulsive, sullen, obstinate, and quite devoid of interest in himself and his surroundings.

On October 31, 1919, he developed a pyrexia with symptoms of influenza and on November 5 he was found to be suffering from lobar pneumonia, from which he died, at 1.20 p.m., on November 6, 1919—seventeen months after admission to Long Grove.

Post-mortem Examination.—State of nutrition: Good. Brain: Weight, 1,158 gm.; convolutions irregular; badly developed. Right lung: Solidified throughout; red hepatization. Left lung: Solidified and red hepatization at base. Heart: Walls dilated; blood-clot in auricle. Liver: Enlarged and fatty. Kidneys: Congested. Testicles: Right, 13.8 gm.; left, 15.8 gm. Other organs normal.

Cause of death, acute lobar pneumonia.

Microscopic Examination of the Brain.—By hæmatoxylin and scharlach and Herxheimer scharlach methods for fatty granular degeneration: Comparatively to the dementia senilis there are few of the cortical cells which show the granular fatty degeneration in the motor area. In the frontal region, however, a large number of cells, small, medium and large, of all the layers, show fatty granular degeneration. The nuclei of the cells are swollen, the nuclear membrane infolded or irregular in outline and the contents often show fine orange-stained granules. The nucleolus may be stained purple or orange red.

Medulla Oblongata.—The cells of the ventral nucleus of the vagus and the nucleus ambiguus show the fatty granules in them. There is very little evidence of change in the hypoglossal. In some of the cells the nucleus is obviously swollen and shows degenerative changes. This applies to all cells including those of the olivary body, although the pigment in this kind of cell is finer. The large cells show the lipid granules better.

Unstained Specimen of Medulla.—Many of the cells show fine granules faintly but not nearly so many as in the stained specimens. The conclusion is that this is a fatty degeneration as the granules stain with scharlach "R." Very few cells of the pons show any fatty change at all.

Paraffin Sections.—By eosin and toluidin blue and toluidin blue alone.

Cortex, Motor Area and Ascending Parietal.—There is a deficiency of basophil substance generally. The Nissl granules in the majority of cells where these granules are well seen in the normal, are in the sections deficient, and there is a tendency, in a varying degree, of conversion of the granules into a dust-like condition. Many of the large motor cells show yellow pigment granules. In some the nucleus is eccentric. As regards the medium and smaller pyramids, many show swollen nuclei, chromatolysis, shrinking of the cell and disappearance of the dendrons or dendritic processes. The cytoplasm often show yellow or unstained granules due to the lipoid substance having been dissolved out. The most marked changes are seen in the deep polymorphic layer where there is hardly a normal looking cell to be found. The nuclei are swollen, in many instances they occupy nearly the whole of the cell. The membrane is often infolded and the nucleus itself very frequently has a pale granular appearance as if it had undergone fatty degeneration and the fat had been dissolved out. The cytoplasm contained but little basophil substance and is filled with minute granules or vacuoles, due to the lipoid having been dissolved out. The processes of the cells are either not seen or are broken off. There is a proliferation of neuroglia nuclei, faintly stained with fine blue chromatin granules. These are seen at all levels, but especially where the cell changes are the most marked. In the ascending parietal convolutions, where the intercalary cells form a definite layer of granules it was observed that these cells have large swollen nuclei, faintly stained blue or pink, according to the stain employed and with but very little cytoplasm. It was observed that the cytoplasm contained little or no chromophylous substance and was filled with fine vacuoles.

Cerebellum.—The cerebellum is well stained; both the cells of Purkinje and the granules give a good basophil stain and this structure might almost pass for normal.

Medulla Oblongata.—Most of the cells of the various nuclei have abundant basophil substance. The Nissl granules however are not so sharply defined as in the normal. Some of the cells show deficiency and a tendency of the granules to break up into dust. A few of the cells show swollen nuclei and vacuolation of the cytoplasm of the cells. These early changes are best observed in the ventral nucleus of the vagus. There is some proliferation of the neuroglia cells especially about the floor of the fourth ventricle.

Pons.—The pontine cells of the first type show a diminution of basophil substance and disintegration of Nissl granules to a variable extent; lipoid granular change in the cytoplasm, especially in the cells with a swollen and often irregular shaped nucleus. The small intercalary cells have very pale nuclei and are difficult to differentiate from the glia cells which are proliferated and exhibit a similar pallor and lack of basophil substance.

Optic Thalamus.—In the thalamus the large medium and small sized cells are all affected with the nuclear and granular change described (*vide* Plate I). The small intercalary cells are similarly affected to those in the pons and one can see the nucleus surrounded by a finely granular cytoplasm.

Corpus Striatum.—The large cells are far less numerous. The changes are the same as have already been described in other cases. Even more marked nuclear and cytoplasm degeneration is to be seen. Oxychromatin reactions in the nucleolus and substance of the cell after staining with toluidin blue and eosin, the granular change in the cytoplasm is seen and the processes of the cells are broken off.

In the Island of Reil the nuclear and cytoplasm changes are well marked especially in the polymorph layer. It is evident also in most of the cells of the pyramidal layer. There is a proliferation of glia cells throughout the cortex. By Victorian blue there is no evidence of proliferation of neuroglia fibrils.

Angular and First Temporal.—Both the temporal and angular regions of the cortex show little difference in the number of cells or their arrangement in columns from the normal. The granular layer is well marked. Stained with toluidin blue and eosin all the cells, under low power magnification, seemed to be stained purple. The same is seen in the angular cortex, though perhaps not quite so marked as was found in the auditory. The large and medium-sized pyramids seem to be less affected but the granular change is quite evident in the smaller pyramids and well marked in the infragranular polymorph layer (*vide* Plate I).

Calcarine Fissure.—Under a low power the cell arrangement appears normal. Although most of the small and medium-sized pyramids of this region show a granular change in the cytoplasm and a swollen nucleus, the most marked change is found in the intercalary cells; which when stained by Nissl method are quite a pale blue. With toluidin blue eosin the nuclei are stained pink and the nucleoli also.

Occipital Pole.—Exactly the same change is observed here as in the calcarine fissure.

Superior Frontal.—Rather a patchy arrangement is observed under a low power in the cells of the supragranular layer, as if there were a deficiency of development. The regular arrangement in columns is not maintained. The apical processes are obliquely set to the surface and the cells themselves seem to have their processes broken off. All the cells seem to take a pinkish tinge; this is especially noticeable in the small cells (*vide* Plate V, fig. 3).

The impression gained from this examination is that the frontal region is more affected than the other parts of the cortex examined, and there is a deficiency of development. Examination by the high power shows the same cell changes described elsewhere in the brain, but in a more advanced degree. In some instances the cells seem to be almost completely destroyed. The nucleoli all take the red dye. Here and there are patches where only glia cells are seen. With Victorian blue no definite evidence of neuroglia fibril proliferation can be observed.

Frontal Pole.—By low power there is less evidence of change than in the superior frontal, still there is not the normal arrangement in columns. Observations with high power magnification however show an advanced nuclear and granular change of the cells similar to those seen in the superior frontal. Frozen sections of the tip of the pole of the first temporal convolutions stained by scarlet and hæmatoxylin, show marked granular degeneration of the cells of the deeper layers. Fat granules are seen in the perivascular spaces of the smallest vessels; some apparently taken up by the endothelial cells (*vide* Plate I).

Adrenal.—By scharlach-hæmatoxylin. The cortex is narrower than normal. The greater portion of the cells have no lipid content. Those that have are stained a deep red. It is possible that this deficiency of lipid is due to the pneumonic condition from which he died, but the narrow cortex and low weight (right, 30 grm.; left, 45 grm.), for a young man is abnormal. The cortex seems to be more deficient than the medulla (*vide* Plate IV).

Testes.—No spermatozoa were found in films made from emulsion of the testes. Sections of the testes stained by scharlach and hæmatoxylin show some deficiency of lipid in the Sertoli cells, and thickening of the basement membrane. There is no evidence of spermatogenesis, and many of the tubules are apparently atrophied.

CASE II.

Clinical Notes.—R. D. G., aged 20. Admitted Colney Hatch, April 27, 1914. Died October 20, 1916. Has a brother in Hanwell (said to be an epileptic), admitted June 10, aged 21. When admitted he was certified as suffering from delusional insanity. He adopts fantastic attitudes, gesticulates freely and hears voices of imaginary persons and claims to be in close communication with the Almighty. He says that he has been dead but has risen from the grave. He was in ex-7 standard at school. He had night

horrors as a child and sleeplessness due to hallucinations. He has been a boot-repairer. In the frequent notes taken during the twenty-eight months of his residence in the asylum there is no statement that he masturbated. The diagnosis was changed in April, 1915, to dementia præcox. He is dull and stupid and very rarely speaks to anyone. He is disorientated for both time and space, extremely untidy and faulty in habits. Further notes: Nothing except that he is occasionally troublesome. June 2, 1915: First stage of tuberculosis. September 18, 1916: Another attack of so-called apical pneumonia. Death from acute pulmonary tuberculosis, October 20, 1916. Testes, 15 gm. and 16 gm. No spermatozoa seen by dark ground examination. Vesicula seminalis seen by dark ground examination.

Microscopic Examination of Testes.—Examination of frozen sections stained by hæmatoxylin and eosin. No spermatozoa seen in sections. Many of the tubes atrophied and only show sustentacular cells, the spermatogonia spermatocytes and their nuclei are absent; the basement membrane is thickened and the fibrous interstitial tissue increased; the interstitial cells are seen but they appear to be smaller than normal as if in the resting stage or partial resting stage. The majority of the tubes show spermatogonia and spermatocytes with active mitotic figures, but spermatids are rarely seen and nowhere could I find any spermatozoa.

Interstitial lipoid: hardly any lipoid seen. Very little in cells of tubes. Examined with high power, fine granules seen in syncytial (Sertoli) cells.

Examination of Brain.—Weight of brain, pons and medulla after hardening in formol until September 15, 1919, 1,210 gm.; deduct 10 per cent. increase due to hardening, 121 gm.; = 1,089 gm. net weight. The weight therefore is considerably below the average weight of the male brain.

Microscopic Examination of Brain: Frontal Lobe.—Toluidin blue and eosin. The majority of the cells are stained a rather faint purple. There appears to be a failure of cells groups in pyramidal layer as if undeveloped. In these regions the glia cells are in excess with very pale stained nuclei. The nuclei of the neurones are large, clear and irregular in outline. The nucleoli and intranuclear network are not so well-stained as normal. The intranuclear network is stained pink and the nucleolus is frequently stained purple instead of blue. The cytoplasm is either stained a diffuse purple or a faint pink. As a rule the larger the cell the more blue is seen in the stain. Nowhere is there evidence of Nissl granules. The granular and infra-granular layers show the most imperfect staining under a low power. With an oil immersion the nuclear change is most pronounced in these cells. A great proliferation of glia cells is seen, many of which can be seen adherent to the degenerating neurones—not a normal cell could be seen. The glia nuclei are as in other cases only faintly stained.

Superior Frontal Lobe.—Very marked nuclear change in all the cells both large and small. The cytoplasm of the large pyramids shows no Nissl granules. The edges are crumbling, the substance is diffusely stained. There are many neuroglia cells—some of them lying in the perineuronal spaces.

Motor Area.—A number of the large Betz cells show well marked nuclear changes. In others the nucleus appears normal, although there is usually a deficiency of the chromatin substance. A great many satellite cells are seen around the neurones. In other respects the changes in the cells of the various layers resemble those described as occurring in the frontal lobe—except that the change is not nearly so marked and there is no evidence of failure of development of cells.

Occipital Cortex.—Similar changes of nucleus and cytoplasm in cells observed only not so marked. Both granular layers show very pale staining. The cells have a large swollen clear nucleus, the whole stained a purple pink, the cytoplasm is more evident and exhibits less crumbling and disintegration than the cells in the frontal lobe.

Cerebellum.—Strikingly evident under a low power is the deficiency of chromatin in the granule cells. There are patches and streaks of faint blue or purple staining. These patches can be resolved under a high power and show in their midst very faintly stained nuclei. The cells of Purkinje are generally of normal shape, but exhibit as a rule only fine Nissl granules. Generally speaking, the cells are stained a diffuse purple with the polychrome or double stain.

Examination of Brain for Lipoid Granules in Cells.—Frozen tissue sections, stained by scharlach and hæmatoxylin. Cells of optic thalamus: A great many of the larger and medium sized cells show lipoid granular degeneration of cytoplasm. Frontal lobe: Nearly all the cells of the various layers show lipoid granular degeneration. Motor area: Little or no degeneration seen; only a few cells of deeper layers show some lipoid granules. Medulla: A few of the large motor cells show slight lipoid degeneration.

CASE III.

History.—D. B., an unmarried labourer, aged 33. He was admitted to Claybury Asylum on May 15, 1903, suffering from melancholia. He was sullen, reserved and obstinate, seldom speaking except in answer to imaginary voices addressing him. At times he struggled with the attendants, but seemed to have no recollection of same. He had no idea of time or place and his memory was very bad, so bad that he did not know what occupation he had followed. He also suffered from marked delusions of persecution and thought his food was being poisoned. He stood for long periods of time in the same place and position. He was in a poor state of health, but his heart and lungs and other viscera were reported healthy. The progress notes up to August, 1908, when the patient eventually died of pulmonary phthisis, report a state of progressive dementia. In April, 1905, he was said to be simple, childish and laughing without cause and at other times suffering from great depression with aural hallucinations and delusions of persecutions.

Microscopical Notes.—Weight of brain, 1,250 grm. Nissl polychrome: Basal ganglia, small and large cells show characteristic nuclear change

(nucleolus looks red). Considerable increase of neuroglia cells, pale colour (deficient nuclein), many in groups around degenerated cells.

Medulla.—Polychrome. Very characteristic nuclear and cytoplasm changes throughout. The large cells of the hypoglossal are least affected. The large cells of the ventral nucleus of the vagus are much affected, the small cells of the dorsal nucleus are much affected, and all the small cells of the medulla, in varying degrees, show the characteristic changes. The neuroglia cells are proliferated and although there is deep staining of the Nissl granules, especially in the large motor cells, nevertheless the nuclei of the neuroglia are very pale pink, giving therefore an oxychromatin reaction.

Cerebellum.—Purkinje cells are well stained with the basic dye blue, but the granules are poorly stained by the basic dye a purple pink. The intranuclear network is very distinct and is so stained.

CASE IV.

History.—J. G. H., admitted to Claybury Mental Hospital on May 24, 1904, said to be suffering from mania. He had been a clerk by occupation: his age was 27 and he was unmarried. He had led a temperate, steady life and shown considerable ability and aptitude for his work while at school. Fifteen months prior to admission he suffered from religious excitement; expressed desire to become a missionary and to reform the East End of London. On his father's side of the family there was a history of intemperance and mental weakness and one of his aunts was an epileptic. He began wandering aimlessly at nights and staying out late. When he was admitted to Claybury he suffered from delusions of persecution, aural hallucinations and expressed strong religious convictions. At first he was a very difficult patient to deal with, he attempted to escape and had to be shut in a strong room. Later he developed a suicidal tendency, but this soon passed off. He became much less impulsive and much quieter. In January, 1905, he was diagnosed as adolescent mania and was much more resistive and restless about this time. In 1907 he was for some time (months) very troublesome, striking and teasing other patients, but gradually he was becoming more simple and childish and grinned and grimaced in a meaningless fashion. After a few months of more marked dementia the patient caught cold, developed broncho-pneumonia, and after four days' illness died on September 25, 1908.

Microscopic Notes.—Weight of brain, 1,590 grm. Tip of frontal convolution, Nissl stain: Every cell shows characteristic degenerative changes. Swelling of nucleus, infolding of membranes, pallor of nucleolus or reddish colour, vacuolation, granulo-pigmentary degeneration, disintegration of cytoplasm, shrinking of cell, no great amount of neuroglia cell proliferation, pallor of glia cells. No vascular changes. The most marked cellular change I have seen. Nissl cerebellum: Granules faintly stained comparatively. Purkinje cells: Nuclear swelling and infolding of nuclear membrane; nucleolus pale or reddish colour. Chromatolysis more marked in some cells than others. Nuclear change marked in some cells and yet little chromatolysis.

CASE V.

History.—C. O'C., aged 22, employed as a domestic servant. Attack commenced about fourteen months previous to admission, but she had gradually been getting worse during the last three months. No further previous history obtainable. On admission to Horton Mental Hospital, April 16, 1903, she was diagnosed as a case of melancholia, her mental condition being very dull, with hallucinations and an impaired memory. Her bodily condition was fair. Both bodily and mental condition remained unchanged until March, 1907, when she was re-certified and diagnosed as suffering from dementia præcox. She was then stuporose, dirty in her habits, and showed marked katatonic signs. Her health continued fair. On February 14, 1908, she had a very violent outburst, developing a tendency to attack anyone in her vicinity. This was followed by a condition of stupor in which a foul stomatitis developed. She was removed to the infirmary. Her pulse became rapid and weak, and her temperature became subnormal. A cough and dullness at bases of lungs developed; also signs of peripheral neuritis of the legs. On March 8, 1908, she collapsed with a very subnormal temperature and extremely feeble pulse, and died at 9.35 p.m. of the same day.

Post-mortem Examination.—State of nutrition: Poor. Lungs: Oedema and congestion of bases with muco-pus in small tubes. Heart: Marked fatty degeneration with some infiltration and pigmentary change. Aorta: Slight atheroma. Liver, spleen, kidneys and small and large intestines were congested. All other organs normal.

Cause of Death.—(1) Fatty degeneration of heart; (2) bronchitis.

Microscopic Examination of Brain.—The following structures were examined: Medulla oblongata, top of first frontal, top of ascending parietal. The staining employed was polychrome. The sections were examined about ten years after they had been made. The tissue had been alcohol-fixed and the sections had retained their coloration perfectly. Medulla oblongata: All the cells show marked changes. Nissl granules are absent. The cytoplasm is shrunken and contains a basophil staining duct; there is vacuolation of the cytoplasm indicating that lipoid granules in abundance had been present but dissolved out. The nuclear changes in greater or less degree were present in the majority of the cells. In many (especially the smaller) cells the nucleolus is stained a faint pink. The nucleolus instead of giving a blue stain is either pink or purple. The same changes only marked if the cells are observed in the two cortical structures above named. The glia cells stained faint pink are proliferated. In the ascending parietal the granule layer is especially affected. The small cells show a large swollen pink nucleus with a vacuolated ragged surrounding of cytoplasm. The polymorph layer of cells show well marked changes of the cytoplasm and nucleus. The cortex only measures 1 mm. instead of 2 mm. in depth. The frontal top: The columns of Meynert are not disorganized. The pyramidal cells show the apical processes well, and under a low power the section might pass for normal. Under high magnification

the most pronounced and typical changes in all the cells are seen, especially marked is the change in the polymorph layer. The following changes were observed: Complete absence of Nissl bodies; great diminution of basophil substance in the cytoplasm, leaving an irregular vacuolated structure. Some of the vacuoles contain yellow lipochrome granules, others obviously have contained a lipid substance that has dissolved out in the preparations of the sections. Some of the cells are mere shadows. The nucleus is swollen irregular in shape, membrane often infolded or crenated. The nucleolus is stained pink or purple in many of the cells. There are large numbers of pale slightly pink-stained neuroglia cells. These can often be seen adherent to the dead or degenerating nerve cells. The dendritic processes are broken off and not a healthy normal cell can be seen. The changes are most marked in the polymorph layer.

CASE VI.

History.—M. R., aged 17. No history prior to admission given. Admitted to Horton Mental Hospital on August 29, 1907. She was in a stuporose condition and took no interest in her surroundings. It was with difficulty that she could be made to open her mouth or eyes. She was in a very weak state, with discharging sinuses round left shoulder and signs of consolidation of left lung. Pyrexia was maintained, and she became slowly weaker, developing signs of cavity in her left lung, and her right lung was also affected. Her mental condition was at first one of katatonic stupor. At night she became noisy and restless, later she was more or less stuporose. Patient became rapidly weaker, and finally died at 5.12 a.m. on January 4, 1908.

Post-mortem Examination.—State of nutrition: Very emaciated. Both lungs: Consolidated with tubercle: in both upper lobes there was a large cavity. Small intestines: Tubercular ulceration throughout. Organs of generation: Both tubes much enlarged, matted together and full of caseous material and slightly adherent to surrounding structures; caseous material in body of uterus indicating tubercular disease. Joints: Tubercular disease of shoulder joint; other organs comparatively normal.

Cause of Death.—(1) Tubercular salpingitis; (2) tubercular disease of lungs, intestines, and left shoulder-joint.

Microscopic Examination.—Polychrome and eosin. Methylene blue and eosin-stained sections of the cortex in various regions. The corpus striatum, optic thalamus, medulla oblongata, and cervical spinal cord were examined. The cells of the cortex in various regions, especially the frontal, show changes of a primary degenerative character. The columns of Meynert, as a rule, are seen, but the cells generally speaking are deficient in basophil staining reaction. The outline is irregular, the processes are short, and the apical processes are only clearly defined for a short distance. The nuclei show signs of degeneration. They are swollen, and the nuclear membrane is infolded or crenated; the nucleolus and intranuclear network is stained a purple or red. The deeper layers of polymorphic cells are more affected than the superficial

layers of pyramids. Both the corpus striatum and the optic thalamus show similar changes in a marked degree. The intercalary neurones of the cortex and the basal ganglia give an oxychromatin reaction. The neuroglia cells are likewise affected, the nuclei staining pink instead of blue. They are increased in numbers, especially around the more obviously degenerated neurones. Similar changes are found in the medulla oblongata, even the large cells of the somatic nuclei show a marked diminution of the basophil substance (*vide* Plate V).

CASE VII.

History.—C. J. H. Admitted to Bexley Mental Hospital on September 14, 1901, aged 23. No history, prior to admission, except that he cut his throat in an attempt to commit suicide; that he reached Standard IV at the age of 13; and that the onset of the mental condition occurred fourteen months previously.

Condition on Admission.—Poor physical development; except for a slight general bronchitis, the organs were normal.

Mental Condition.—Attention was difficult to obtain and retain, and he was intellectually dull. Comprehension was poor and reaction most erratic and absurd. His memory was also poor, especially for recent events. He was eccentric, self-absorbed and entirely controlled by his hallucinations and delusions. He apparently believed he was related in some mysterious manner to the Heavenly spirits, as he denied all relation to human social classes. He was not depressed, neither was he resistive or hostile. Diagnosed as a case of recent melancholia.

His manner developed into restlessness, noisiness and hostility at frequent intervals, when he attacked fellow patients and attendants. Between these relapses he was quite amenable, and did some useful work in the wards, but was never reliable.

On January 30, 1908, his mental condition became much worse. He was very dull, confused, emotional and depressed. At times very hallucinated, resistive, restless and inclined to be hostile. Health remained fair.

On February 23 he developed hyperpyrexia, and was found to be suffering with acute lobar pneumonia, from which he died at 8.12 a.m. on March 2.

Post-mortem Examination.—State of nutrition: Poor. Right lung: Normal. Left lung: Consolidation of the whole of the lower lobe; grey hepatization; recent dry effusion over the lower lobe and the base of the upper lobe. All other organs normal except for some congestion of the liver, kidneys, and small and large intestines. No tuberculous or dysenteric lesions.

Cause of Death.—Lobar pneumonia.

Microscopic Notes.—Polychrome stain tip of first frontal. Very marked granulo-pigmentary degeneration of all cells (both first and second type of Golgi), proliferated neuroglia cells with pale nuclei. Top of ascending parietal granular layer, swelling and oxychromatin reaction of nucleus, very marked characteristic degeneration of supra- and infra-granular pyramids, more marked

in the infra-granular region. Extreme pallor of neuroglia cells, of which there is some evidence of proliferation. Basal ganglia: All stages of degeneration of cells up to disintegration and complete destruction, the same and as intense as in the cortex. Groups of neuroglia proliferated cells stained pale pink. Cells of second type of Golgi are undergoing degeneration, for they are studded with small pale granules in many instances.

Medulla Oblongata.—Although the Nissl granules are well formed in the hypoglossal cells, the nuclei are obviously changed; they are swollen up—the nuclei are pink or purple, the glia cells have undergone active proliferation but give a pale pink oxychromatin reaction. The cells of the vago-accessorius nucleus show the characteristic changes even more markedly, most of the cells exhibit marked chromatolysis as well as the nuclear change. At a lower level the cells of Burdach's nucleus show marked nuclear changes and chromatolysis. Most of the cells of the olive show a granulo-pigmentary degeneration of the cytoplasm.

CASE VIII.

History.—R. R. B., aged 21. Educated at a Board School, where he showed considerable literary ability but little mathematical ability. He was employed on the staff of several papers, in a minor position, and recently had been reporting for a sporting newspaper. As a lad he was excitable, restless and masterful. There is no history of fits, and the family history is said to be good; the father is intelligent and the mother appears to be a sensible woman. About four months ago patient acquired ideas of persecution on the part of other reporters on the staff of the paper, believing that they accused him of being illegitimate and the son of a member of a noble family. He suffered from aural hallucinations. Later his delusions developed; he became possessed of the idea that his home was an immoral house, that the infirmary was full of prostitutes, and that he himself was suffering from syphilis. He thought loafers in the street made remarks about him as he passed, and he frequently challenged men to fight. He became apprehensive and depressed, believing that his only relief would be either by committing suicide or by strangling some other person. He had never made any attempt at suicide but had frequently made homicidal attempts.

Admitted to Bexley on May 4, 1908. Certified as a case of dementia præcox. In his manner he was stereotyped and somewhat aloof, but he recounted his tales clearly and briskly. Consciousness was clear, apprehension was satisfactory. Intelligent and active-minded; memory good. His moral habits appeared to be unexceptionable. He made many violent attacks upon both patients and staff, and was confined to bed in a single-room during the greater part of his residence here. On several days he was in a state of great excitement, intermissions on these days being few and short, but for the most part he was quiet; his outbursts have been suddenly aroused and as suddenly subsided. He made one attempt at suicide after admission. During the past six weeks he was as a rule depressed, dull, uncommunicative and somewhat

retarded, and during the last fortnight he became very feeble and emaciated. On the night of August 8, 1908, he suddenly collapsed, and died at mid-day on the 9th.

Post-mortem Examination.—State of nutrition: Slight emaciation. Left lung: Deeply congested and shows patches of broncho-pneumonia. Heart: Slight recent endocarditis on edges of left mitral valve; few patches of atheroma of aorta just above the valves. Adrenals: Enlarged. Large intestines: Enlargement of the mucous follicles, but no dysenteric lesion. Other organs comparatively normal. No sign of tubercular disease.

Cause of Death.—Broncho-pneumonia.

Microscopic Examination of the Cortex Cerebri.—By Nissl and hæmatoxylin eosin methods. The superior frontal, ascending frontal, orbital, lingual, Broca, tip of inferior frontal examined. All these structures were without noteworthy vascular changes, but they all exhibited marked cellular changes and neuroglia cell proliferation. The cellular changes were as follows: Deficient cellular development in the frontal lobe (excepting ascending frontal). And in this region the cells show more marked changes; the columns of Meynert are disorganized, the cells have their dendrons broken off, few show any apical pressure, the cytoplasm is vacuolated, doubtless due to the lipoid granules having dissolved out in the paraffin embedding process; the nuclei are swollen and the membrane often infolded or crenated. These changes are seen in the other regions of the cortex but to a less degree. The cells are generally shrunken and show a marked degree of chromatolysis. Nissl granules are seldom seen even in the large pyramids.

CASE IX.

History.—E. C. Patient was admitted to Hanwell Mental Hospital on May 27, 1914, at the age of 73, suffering from senile dementia. Her condition on admission was one of feebleness, restlessness and depression. She was evidently in a state of considerable trepidation as to her future, and believed that dogs were to eat her. She was incapable of coherent conversation and dirty in her habits. Her memory was grossly affected, and consequently no previous history could be obtained. Her sister was a patient in the same Mental Hospital. Her physical condition was comparatively normal for one so advanced in years. She was very feeble, but there was no definite paresis and she was blind in the right eye from cataract. During her short residence at Hanwell she was very childish and had no idea of time or space. She was incoherent and restless and was constantly folding and unfolding her clothes. She was depressed and had some vague ideas of unworthiness, calling herself a wicked woman. She is noted as being the subject of many senile tissue changes. On June 5, she became rapidly weaker with laboured breathing and failed to rally under cardiac stimulants. She continued in a semi-conscious condition and finally died at 9.45 p.m. of the same day.

Post-mortem Examination.—State of nutrition: Wasted. Brain: Marked

wasting; sulci well marked; convolutions rounded and atrophied. Thyroid: Somewhat wasted. Right lung: Lower lobe showed some patches of consolidation. Left lung: Some bronchitis and emphysema. Heart: Walls thin and atrophied; slight atheroma of valves; pigmentary degeneration of muscle. Aorta and coronary arteries: Atheromatous. Liver: Some fatty degeneration. Kidneys: Granular. Renal artery: Atheromatous. Organs of generation: Very distinctly atrophied. Other organs showed no changes worthy of note.

Cause of Death.—Secondary terminal bronchitis and broncho-pneumonia; pigmentary degeneration of heart; chronic granular nephritis.

Microscopical Examination of Brain.—Hardened in formalin, four years. Toluidin blue and eosin. Frontal pole. Cerebellum. Motor area. Medulla.

Frozen sections stained by scharlach and hæmatoxylin show very marked lipoidal degeneration of cortical cells with much lipoid in the perivascular spaces. This condition is especially marked in the frontal region of the brain. The small vessels of the brain do not show degenerative changes. The nuclear changes are not so marked as in the case of dementia præcox. The nucleoli do not give an oxychromatin reaction. A piece of cerebellum embedded in paraffin with a piece of a case of dementia præcox and a piece of a case of tetanus. The three in one block were cut into sections of 10 microns and stained. A naked eye examination showed a deficiency in basophil staining of the cerebellum in the cases of dementia senilis and dementia præcox as compared with the case of tetanus.

CASE X.¹

DEMENTIA PRÆCOX; MONORCHIDY; ATROPHY OF SUPRARENAL ON SAME SIDE.

(*This case, being of special interest, is given in full.*)

G., aged 27, admitted to Claybury Asylum, September 6, 1906. No. 4,846. Single, no occupation. First attack at the age of 23. Duration about ten days; form—subacute mania; previously not in an asylum.

Medical Certificate.—"He fancies people follow him about the streets to annoy him. At times he becomes very violent and noisy, and he then fancies he is surrounded by men and he fights with them and becomes very dangerous. Sometimes he is very sullen and morose and will neither speak nor answer questions."

For the past four years he has shown an incapacity for study, a vacant expression and was careless in his dress. On 30th ultimo he threatened an imaginary person with a knife and then ran into the street. He became apathetic and careless in his work, and has not slept well of late. He had a very good appetite. He was cheerful, but rarely speaks now. He was temperate and an abstainer. Had no religious excitement and was until

¹ I am indebted to Dr. Sano for the notes of this case.

recently a member of South Place Ethical Society. He has an undescended testicle, which some medical men think has retarded his brain development, and others disagree. He passed the Civil Service Examination, but low down on the list. He did clerical work, mostly in accountant's department of G.P.O. He was born and lived at Hackney.

Previous Medical History.—He was not certified, but under the care of Mr. Corner, of Harley Street, from December, 1904, till June, 1905, and under Dr. Forbes Winslow from August, 1905, to February, 1906. He was in different private homes. He was at home since February and had numerous attacks which with some exceptions were not beyond home management. As a rule he was quiet, idle, avoiding exertion. The attacks commence with threats and swearing. He had occasional attacks of asthma.

Family History.—Father: Paralysis agitans past four or five years. Parents not related. No consumption, no intemperance.

Examination of Patient.—Height, 5 ft. 10½ in. Weight, 11 st. Hair fair; patches of hair on sacrum. Absence of left testicle. Palate very narrow and V-shaped. Teeth carious. Bowels regular. Urine 1,008, acid. Pupils equal, react well. He is pale, anæmic and flabby, but otherwise well covered and in fair condition. Knee-jerks present.

On Admission.—To my questions he answers in an off-hand jerky way. There is no retardation. He holds himself in a stereotyped way and shows tendencies to quaint mannerisms. His expression is dull. He seems a little irritable but is otherwise unemotional. He confesses he has no will power. He cannot concentrate on his work. He describes that, as a result of insomnia, he would get up and shout and that he could not help doing this, and suggests that it was an uncontrollable impulse. He has some insight into his case but it is too self centred. Memory and orientation fair.

Subsequent History of G.—September 12, 1906: He is the subject of sub-acute mania. Is sullen and disinclined to answer questions. Believes that there is a conspiracy to persecute him and that he is followed about by people who are plotting to injure him. He is in good health and condition.

December 10, 1906: He is apathetic and has no initiative. He shows no disposition to improvement.

August 3, 1907: He is suffering from dementia. He is dull and confused, lacks all interest in himself or surroundings, is apathetic and has no initiative. Stands for a time in one position. Speaks in a drawling monotone; yawns frequently. He is in fair health and bodily condition.

November 2, 1909: Struck attendant in the mouth causing swelling and cut on inner side of the lip (upper).

August 3, 1910: He hears imaginary voices speaking to him. At times he becomes irritable and excitable and makes homicidal attacks upon those who are near him.

1913: He is suffering from primary dementia.

August 15, 1914: Positive Vidal. Transferred to hospital; no symptoms.

May 14, 1915: He gives evidence of aural hallucinations and responds to a female voice he frequently hears. He is impulsive at times.

February 10, 1916: He has been failing gradually for the last four days. Temperature subnormal. Pulse weak and irregular. Died on this date.

Post-mortem.—Cause of death, broncho-pneumonia.

Left suprarenal: 3.5 gm.; very little lipoid cortex. Right suprarenal: 6.5 gm.; very little lipoid cortex (*vide* figs. 1 and 2).

Right testicle: 12 gm. Left absent. No spermatozoa in testes or vesicula seminalis. The left vesicula seminalis was very large as compared with the right: both contained a thin clear gelatinous fluid but no spermatozoa could be found by dark ground illumination. Testis: No spermatozoa found, tunica albuginea thickened, and the testis presented a whitish appearance. Examined with hand lens: There is excess of interstitial tissue. The white tubules are shrunken in some places, and not so distinctly seen as in others. There is clearly an atrophic process.

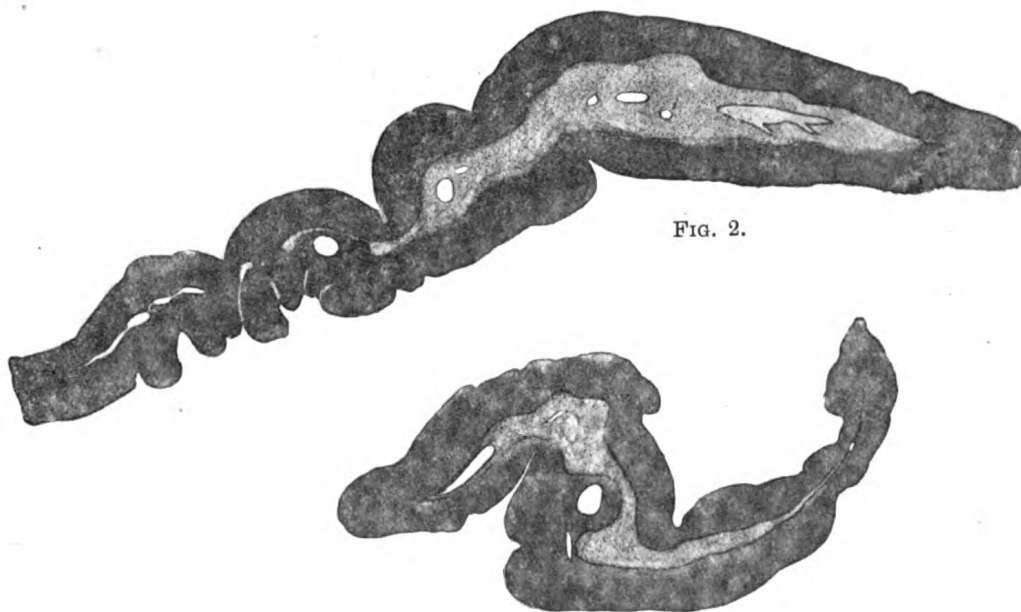


FIG. 2.

FIG. 1.

Sections of (1) left suprarenal, and (2) right suprarenal gland, to show comparative size. (Magnification 12.)

Microscopical examination shows a complete atrophic process of a very advanced nature; most of the tubules greatly thickened basement membrane with clear unstained vesicles filling the lumen. Others show cells filling the lumen, similar to those found in the foetus. Nowhere can active mitosis be seen, nor any evidence of any stage of spermatogenesis (*vide* Plate VI, figs. 1 and 2). The appearances coincide with those found in other advanced cases of dementia præcox.

Heidenhain stain: Tubules all show atrophy, but there is varying degree in the extent of the atrophy; there is no spermatogenesis observable in any of the tubules; in some the epithelium has entirely disappeared, leaving only the thickened basement membrane and hyaline rudiments of the epithelial cells; in other tubes there are epithelial cells, but none show active mitosis. The cells of Sertoli are seen distinctly in many of the tubules, as they form the only remains of the epithelial lining cells. No evidence of spermatocytes or spermatogenesis is observable in any of the tubules. Interstitial tissue (stained with hæmatoxylin and eosin) is increased but there is very little evidence of the existence of the interstitial cells of Leydig. Hæmatoxylin and scharlach stain shows very little interstitial lipoid; there is a considerable amount of dark red coarse lipoid granule substance within the tubules, many of these are in the syncytial cells of Sertoli. Scharlach stain, with a low power, shows that nearly all the lipoid is within the whole extent of tubules, but as if resulting from fatty degeneration of the epithelial cells. There is comparatively little in the interstitial tissue.

Suprarenal cortex stained by the same method shows a great deficiency of lipoid, in some places quite absent, in others in relatively small scattered patches.

Examination of several sections permits the conclusion that there is a marked deficiency of the cortical lipoid substance.

Other cases of dementia præcox showed a diminution of the cortex, and this case is of interest in the fact that the adrenal gland on the side of the absent testicle weighed one half that of the opposite side. The suprarenal gland is developed from the genital ridge, and the cause of the absence of the testis and the very small suprarenal gland on that side was doubtless an embryonic deficiency. There are many facts which show a correlation between the adrenal cortex and the sexual functions which I will briefly summarize.

THE INFLUENCE OF THE ADRENAL CORTEX ON THE GENITAL FUNCTION.

The cortex adrenalis is enlarged during pregnancy and is small in cases of deficient sexual development, and the fact that changes have been described (in the guinea-pig) by Kölmer in the cortical cells accompanying the phases of the œstrous cycle seem to afford evidence of some relationship between the functions of the cortex and the generative glands, but whether this is direct or operates through other ductless glands—such as the thyroid and pituitary—is not known. The occurrence of a connexion between the development of the sexual

organs and that of the suprarenal cortex has been especially insisted upon by Glynn, who is of opinion that the cortex is concerned with the differentiation and growth of the sexual cells. Bulloch and others have recorded cases of adenoma of the adrenal cortex and precocious sexuality.

Analysis of the suprarenals of the pig by Biedl yielded: 74.61 per cent. H_2O , 25.39 per cent. dry residue; of the latter 61.12 per cent. consisted of proteins and 38.8 per cent. lipoids; as this included the medulla the proportion of lipoids must be very high in the cortex.

The darkly refractile lipid contents are composed of lecithin and cholesterol, the latter in the form of esters. The suggestion that the cortex of the suprarenals may be a seat of manufacture of lipoids of the body and related to the formation of the myelin of the nervous system, is supported by the fact that there is a large development of lipid in the cortex during the period of myelination of the nerve fibres of the brain which development is absent in anencephalous monsters. The superadded part of the suprarenal cortex, according to Elliott and Armour, in the foetus does not contain darkly refracting lipoids characteristic of the ordinary cells.

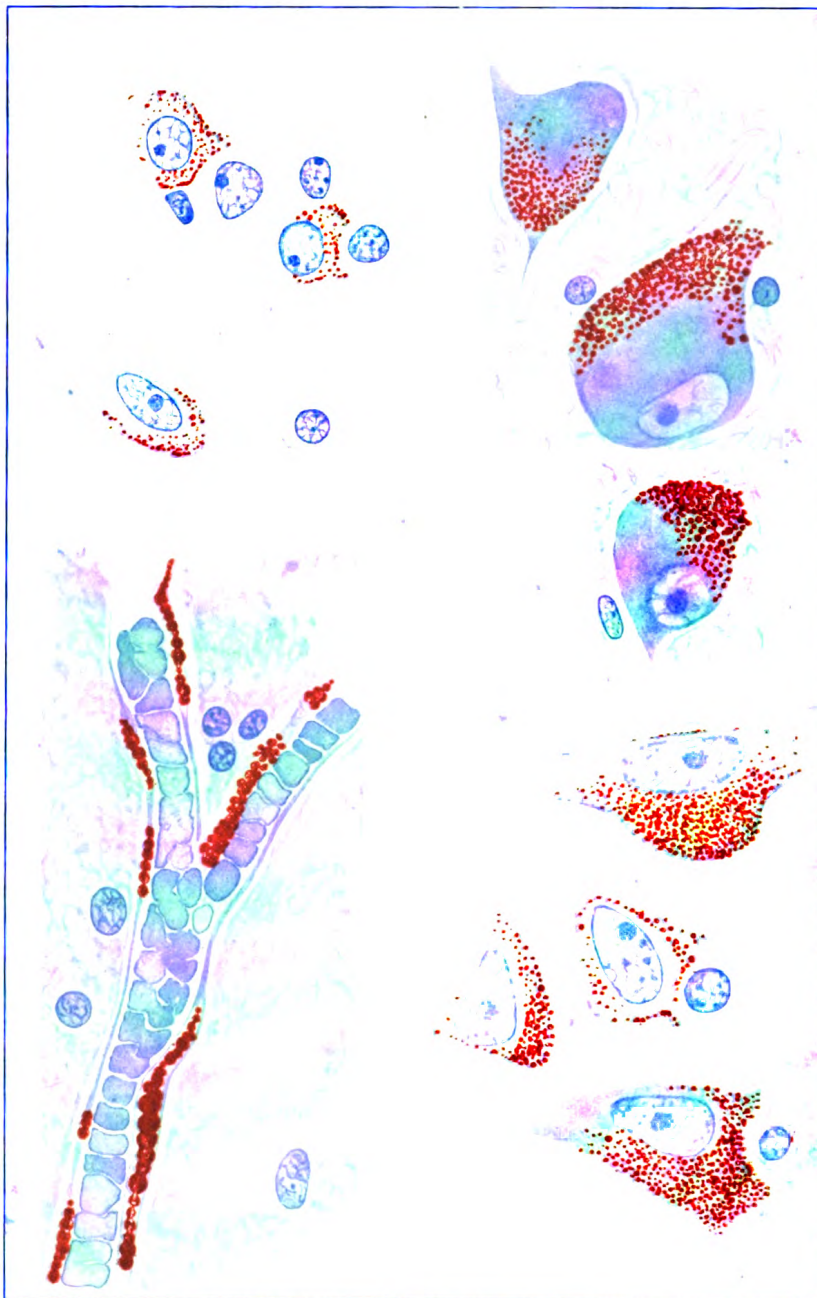
Swale Vincent, in a very interesting paper upon "The Experimental and Clinical Evidence as to the Influence exerted by the Adrenal Bodies upon the Genital System," describes feeding experiments of animals with suprarenal gland and the stimulating influence upon the growth and activity of the testes carried out by R. G. and A. D. Hoskins upon white rats. Other glands did not show hypertrophy. The authors conclude that the testicular hypertrophy is due to the cortical portion of the gland. Swale Vincent is himself conducting experiments in which certain possible sources of error will be removed—viz., he is using only the fresh cortex of the adrenal gland. He points out that drying may de-grease the material and alter or destroy the lipoids.

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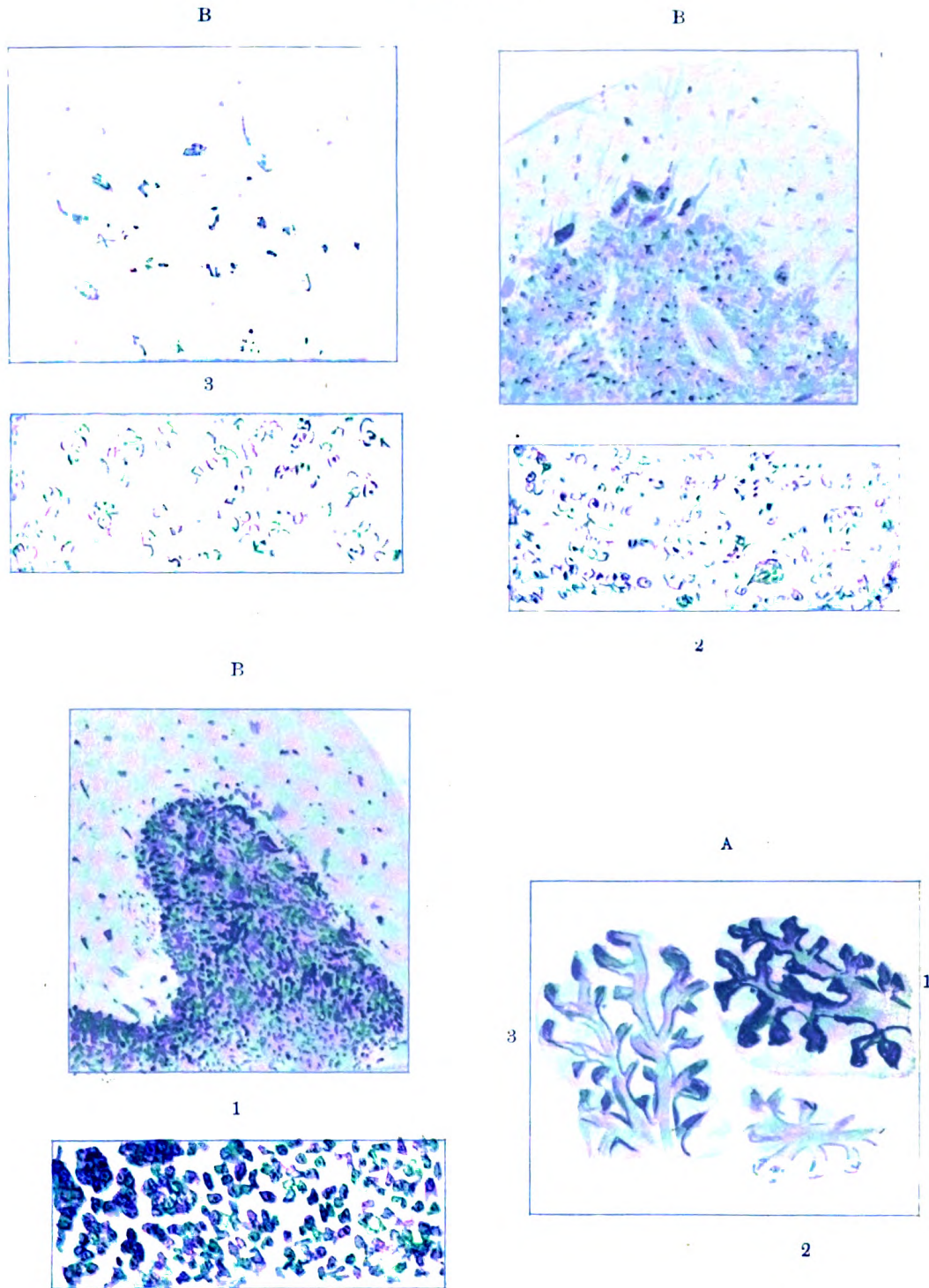
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PLATE I.



Frozen sections of formalin-hardened brain of Case I, stained with scharlach R. and hæmatoxylin mounted in glycerine. To the right are seven large cells of the optic thalamus showing a large number of lipoid granules in the cytoplasm. (Magnification 600.) On the left is a capillary with lipoid granules in the sheath and in the endothelial cells. Above are three cortical cells with lipoid granules and several neuroglia cells. (Magnification 600.)

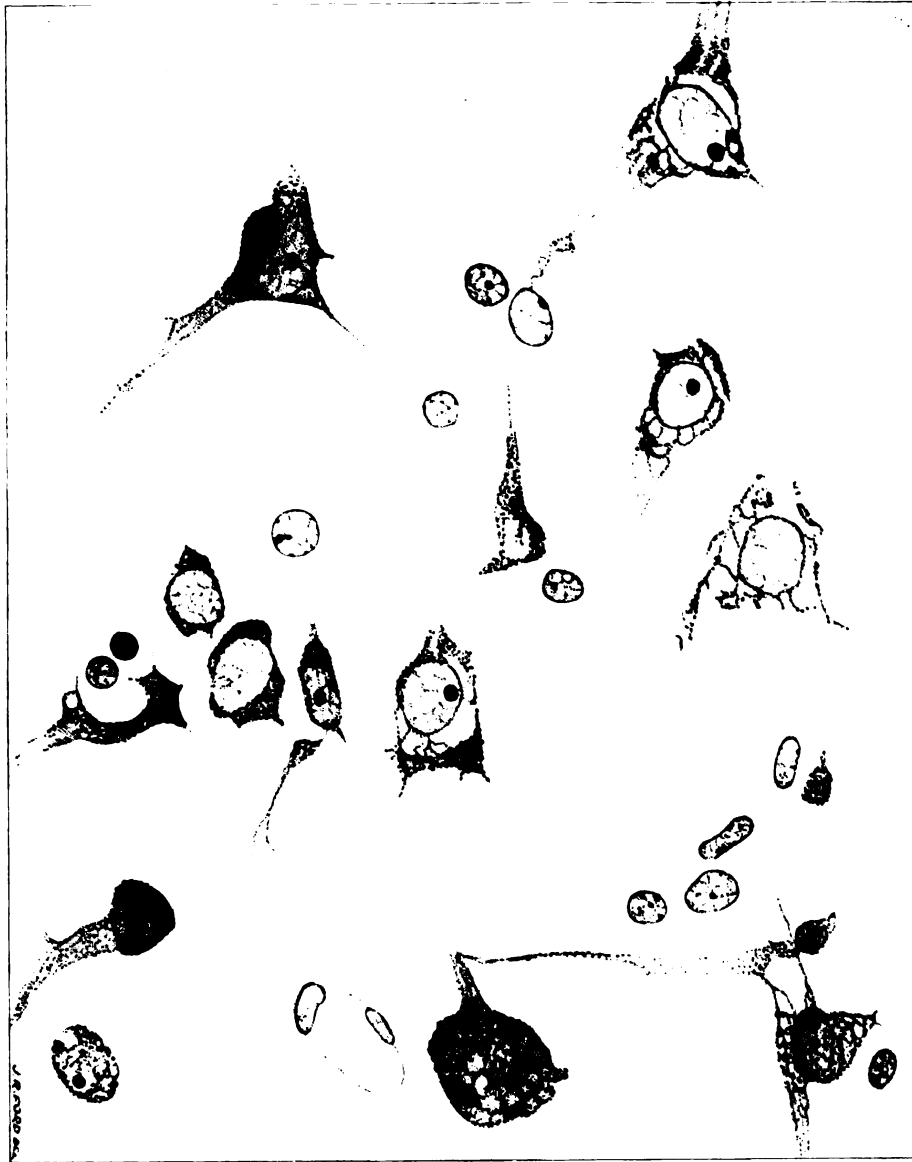
PLATE II.



A, the three sections of cerebellum mounted on one slide (all submitted to the same conditions after removal from formalin), as seen with the naked eye; slightly magnified. Fig. 1, tetanus brain; fig. 2, senile dementia; fig. 3, dementia praecox.

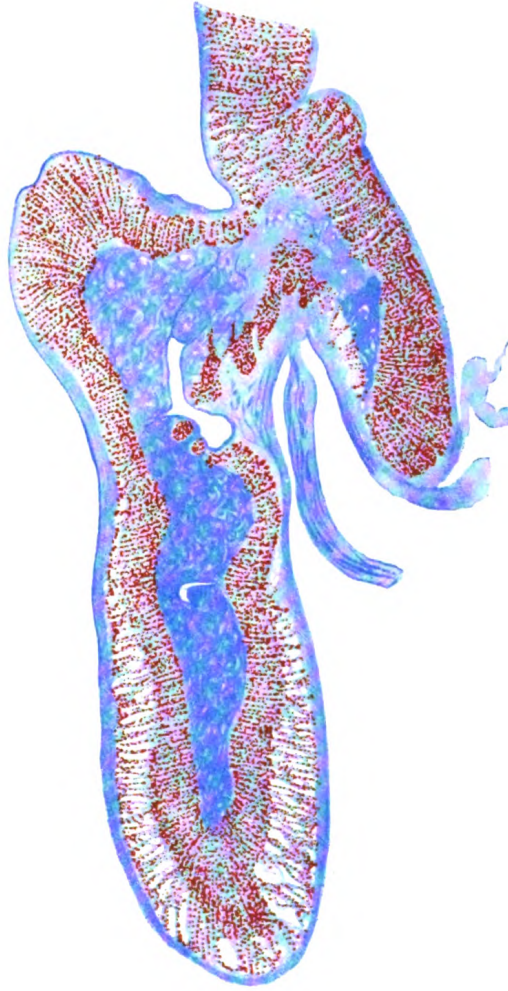
B (1, 2, 3), each of these as seen under the microscope, the upper figure with a low power magnification. The lower, with a high power magnification, shows the granule layer only. Observe the difference in the basophil staining reaction. The only fallacy is the possibility of difference in the formalin employed. Further experiments of a similar nature are being conducted, combined with chemical analysis of the tissues. A more positive conclusion regarding this finding will then be possible; at present it is only very suggestive.

PLATE III.



Section of cortex of angular gyrus (Case I). Degenerated pyramidal cells. Observe the swollen nucleus with intranuclear network. There are no Nissl granules seen, only a purple dust and vacuoles. The nucleolus is stained a reddish purple instead of blue. The neuroglia cells are faintly stained in comparison with the normal. Some of the pyramidal cells are undergoing autolysis, and one shows two neuroglia cells within a hollow space of the cell. Near this is a small stellate cell with greatly swollen nucleus. (Magnification 4, ocular, and $\frac{1}{2}$ oil immersion.)

PLATE IV.



Section of adrenal gland (Case I) hardened in formalin and cut with freezing microtome.
Stained with scharlach R. and hæmatoxylin. (Magnification 12.)

PLATE V.

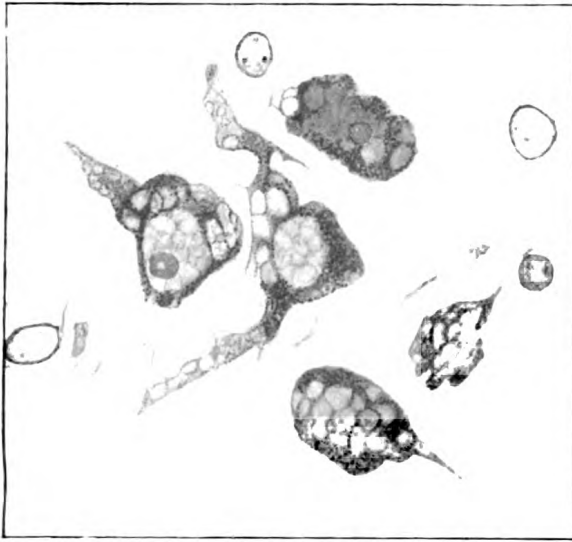


FIG. 1.

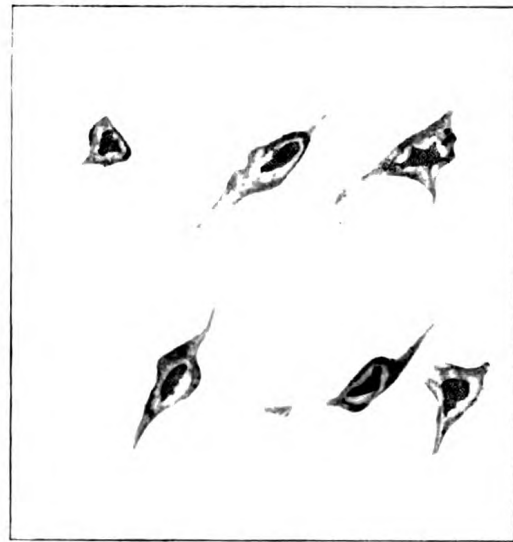


FIG. 2.

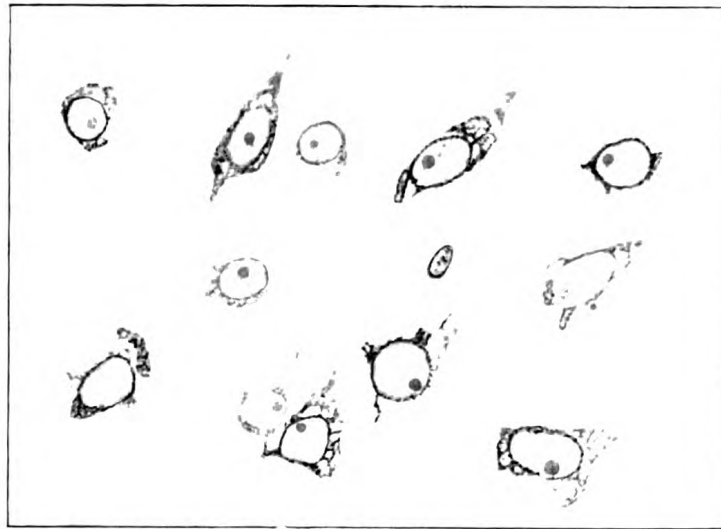


FIG. 3.

Sections of brain of Case VI. Fig. 1 stained with polychrome and eosin. 1, cells of optic thalamus; the nucleus is swollen, the cytoplasm is markedly vacuolated, the processes are distorted or broken off; the nucleolus is stained a reddish-purple. (Magnification 600.)

Fig. 2: Sections of medulla oblongata, degenerated cells of dorsal nucleus of vagus. The nucleus is swollen, and the nucleolus is stained red. (Magnification 600.)

Fig. 3: Section of frontal pole of Case I, stained with toluidin blue and eosin. Marked swelling of the nucleus; the cytoplasm is vacuolated. The nucleolus is stained pink. (Magnification 600.)

PLATE VI.

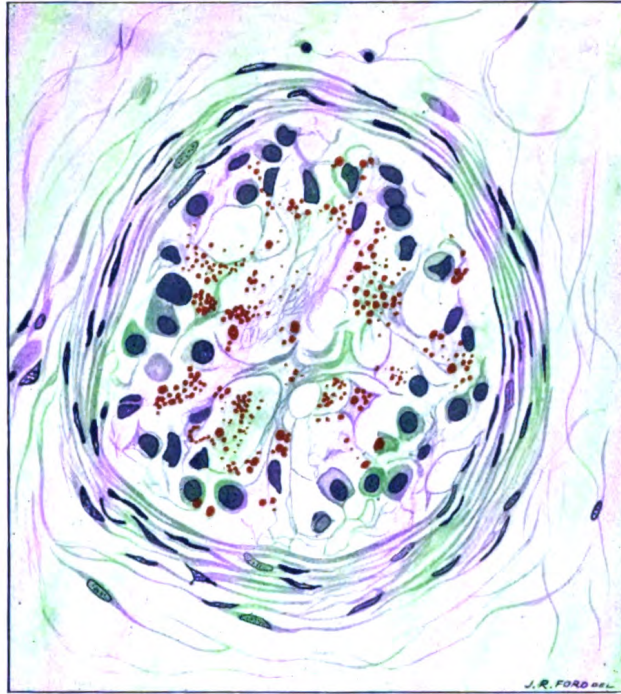


FIG. 2.

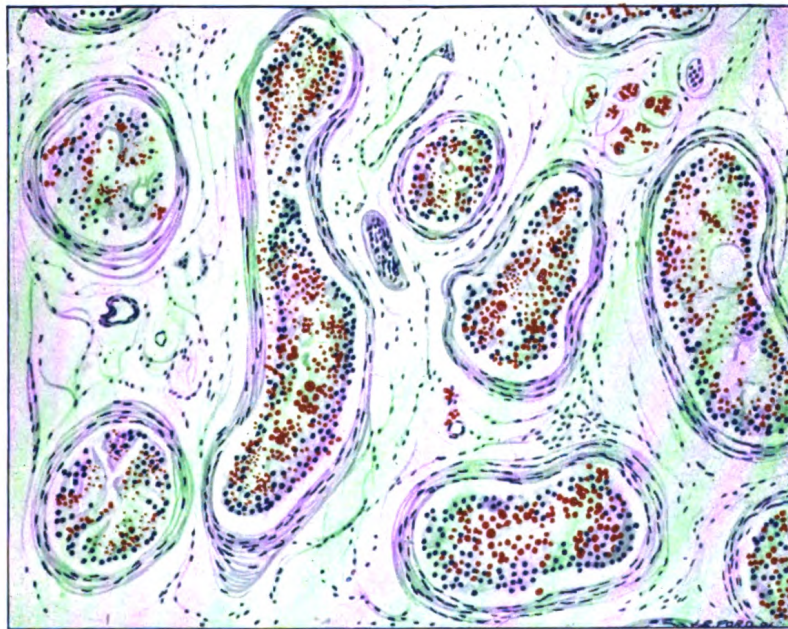


FIG. 1.

Third stage of testicular regressive atrophy. Section of right testis cut by freezing microtome after hardening in formalin. Stained with scharlach R. and hæmatoxylin.

Fig. 1: There is a great increase of the interstitial fibrous tissue; no interstitial cells are seen. The tubules are shrunken; the basement membrane is greatly thickened; there is no sign of spermatogenesis; the lipoid granules are only present in the interior of the tubule. (Magnification 115.)

Fig. 2: A section of tubule magnified 420 times. The basement membrane is greatly thickened; there is no sign of spermatozoa, spermatids, or spermatocytes; the nuclei of the spermatogenic and Sertoli cells present show no sign of mitosis. The lipoid granules are coarse and deeply red stained, and are contained in the Sertoli cells or between them in the sustentacular framework. They are not the normal fine orange-stained granules, and are probably a product of fatty degeneration of the spermatogenic cells.

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Further Pathological Studies in Dementia Præcox, especially in relation to the Interstitial Cells of Leydig.

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PART I.

HAVING in previous communications paid especial attention to the arrest of spermatogenesis and regressive atrophy of the spermatic tubes, and having only made some brief references to the morbid changes in the interstitial cells in various forms of mental disease, I thought it would be of interest to systematically examine, describe and compare the histological appearances of the interstitial cells in the different forms of insanity with the normal at different ages and with one another. The literature is fully considered by Dr. Such in Part II.

THE INTERSTITIAL CELLS OF LEYDIG.

The interstitial cells of Leydig are polygonal in shape with a round nucleus. The cytoplasm of the mature cell is considerable, and contains a substance which takes the eosin stain remarkably well. Consequently sections stained by hæmatoxylin eosin, or Heidenhain hæmatoxylin eosin, show the interstitial cells remarkably well.

I have examined all the material of the hundred cases of patients dying in hospitals or asylums with the view of determining more precisely the condition of the interstitial cells in relation to spermatogenesis.

THE LEYDIG CELLS IN THE PRE-PUBERTAL PERIOD OF LIFE.

At birth the testis consists of the spermatic tubes, made up of a delicate basement membrane containing embryonic, undifferentiated, rather small, epithelial cells, consisting mainly of nucleus with a well-marked chromatin skein. There is abundant loose intertubular connective tissue in which are seen columns, islands and islets of cells, the polygonal outlines of which are quite distinct; the cytoplasm is stained pink, and in the centre is a round nucleus, with a well-developed nuclear membrane containing a chromatin network, both of which are stained deep blue by the basic dye. No nucleolus is visible (*vide* fig. 1). Lipoid granules are visible in many of the cells as revealed by scharlach stained frozen sections, and by vacuoles in hæmatoxylin eosin stained sections mounted in Canada balsam.

NORMAL TESTIS AT BIRTH.

The embryonic tubules, and between them the interstitial tissue, which consists almost entirely of interstitial cells, isolated or in groups, with distinct polygonal outline of cytoplasm stained by the eosin, or a nucleated vacuolated syncytium of what was originally polygonal cells. I shall speak of a syncytium because when the cells are distinctly vacuolated their outline is ill-defined, and they appear to be interconnected. The nuclei in this unstained or faintly stained syncytium are of varied size and shape; many of these are only faintly stained by the basic dye and are deficient in chromatin, and the appearances are not unlike those observed in the regressive atrophy of dementia præcox. Where this is taking place there are a number of more deeply-stained nuclei of fibroblasts. This is the final stage of regressive atrophy. In other places one sees the earlier stage of regressive atrophy, viz., groups of polygonal cells with the cytoplasm faintly stained pink, and the nuclei hardly stained and appearing only very pale blue; in the immediate neighbourhood of these are mature polygonal cells with pink cytoplasm and round nuclei with chromatin network well stained. In these cells which are undergoing regressive atrophy the nuclei instead of being round are irregular in outline, crenated and polymorphic. Here we have all stages of regressive atrophy of the interstitial cells seen in dementia præcox (except pigmentary degeneration), but this is a physiological and not a pathological process. It will be interesting to trace the further stages of the disappearance of these cells after birth.

THE PRE-PUBERTAL DISAPPEARANCE OF THE LEYDIG CELLS.

The Interstitial Cells at Four Months.

Examination of sections of the testis of an infant aged 4 months showed that the tubules are now twice the size owing to proliferation of the embryonic epithelial cells and are closely approximated. This is due to the almost complete disappearance of the interstitial cells of Leydig (*vide* fig. 2 to compare with fig. 1). Sections examined with an oil immersion lens show oval and round nuclei lying in a vacuolated syncytium, but no pronounced eosin-stained cells can be seen. These nuclei are not connective tissue nuclei but the nuclei of the Leydig cells. Frozen sections stained with scharlach show lipoid granules corresponding to the vacuoles. Examination of the tubules with an oil immersion shows numbers of very fine lipoid granules in the syncytium of embryonic cells. The presence of lipoid granules in this situation and in the interstitial tissue and Leydig cells, shows that the formative process is still proceeding, but the size and close proximity of the tubules is indicative of its terminal phase. I have been unable, owing to my not having the material, to trace the stages of regressive atrophy between birth and 4 months and after this time to 10 years.

The Interstitial Cells at Ten Years.

Examination of sections of the testis of a boy aged 10 who died of fracture of the base of the skull. The tubules are not any larger in some portions of the section than those found in the testis of an infant aged 4 months and show no more differentiation of structure. Occasionally one finds the first evidence of differentiation by the appearance now and then of definite spermatogonia and some of the cells show mitotic figures. In some parts of the organ the tubules are closely approximated and the appearances resemble those described as

occurring at 4 months. In other parts the tubules are separated by a considerable amount of interstitial tissue and groups of polymorph oval and round nuclei, like those of immature Leydig cells, can be seen, but only very occasionally can a small polygonal cell with pink cytoplasm and a round central nucleus be observed. The interstitial tissue contains no lipid, for frozen sections stained by Sudan III show no fat in the tubules or interstitial tissue. Function has not therefore commenced in the interstitial cells. As the Sertoli cells do not appear to be present yet, it seems probable that with their appearance the Leydig cells would mature and function, but further observations at later ages are necessary to determine whether this be so. I have taken some pains to show the conditions of the interstitial cells in the pre-pubertal period of life because after birth there is a regressive atrophy and cessation of function, and the appearances presented by the interstitial tissues, at birth and afterwards, in a way correspond to the appearances met with in the regressive atrophy of the interstitial cells in dementia præcox. Moreover, the fact that the development of the spermatic epithelium corresponds with the appearance of lipid in the interstitial cells and the tubules, and its absence with the signs of an absence of formative activity in the tubular epithelium, supports the view that these cells of Leydig perform the double function of providing a hormone and the raw material for formative activity of the spermatic epithelium.

THE LEYDIG CELLS IN THE PUBERTAL AND POST-PUBERTAL PERIOD OF LIFE.

The testis of a boy aged 15, who died from shock of injuries, showed active spermatogenesis, lipid granules in the Sertoli cells and interstitial lipid; this interstitial lipid was found in drops and droplets in the lymphatics and lymphatic clefts, also in the Leydig cells, which have now reappeared in the interstitial tissue. Their reappearance is, therefore, synchronous with the first appearance of the secondary sexual characters which it has been proved they determine.

They were found subsequently at all ages up to extreme old age—80, 85 and 86—though in diminished numbers and corresponding, generally speaking, with the degree of spermatogenic activity, although by no means always, for sometimes these cells could be found in fair numbers while there was little evidence of active spermatogenesis, and the converse. Mr. Kenneth Walker, who has been working in the Maudsley Laboratory on the prostate, has kindly furnished me with the following results, which are in accord with this conclusion (*vide* Table II, p. 24). I am now only referring to cases dying in hospital and to certain asylum cases, but not to cases belonging to the biogenetic psychoses in which there is a partial or complete regressive atrophy.

I came to the conclusion from the examination of the testes of young adult cases dying from shock shortly after receiving severe injury and the testis of the boy above referred to, that these Leydig cells have a comparatively short life and are continually maturing, decaying and being renewed (*vide* fig. 1, Plate I). All stages of small nuclei resulting from active division can be observed, followed by division of the cell and growth to the mature cell, such as was seen in the newborn child. The cytoplasm of the normal mature cell is abundant and is stained by the eosin dye a deep pink, so that with a low power, islands, columns and islets of cells can easily be recognized in the interstitial tissue.

When examined with an oil immersion details can be observed which cannot readily be seen with a low power, e.g., the amount of chromatin in the nucleus

can be gauged and varying degrees of vacuolation in the cytoplasm corresponding to lipoidal contents can be estimated. I have come to the conclusion from my observations that vacuolation and disappearance of the pink cytoplasm is associated with a tendency to make the outline of the cells ragged or indistinct; and if marked, to convert the island of cells into a nucleated pale vacuolated syncytium.

THE LEYDIG CELLS IN PROLONGED SEPSIS.

I found this pale vacuolated syncytial condition in various cases of prolonged sepsis such as suppurative pericarditis with empyema, cerebro-spinal meningitis and several cases of gunshot injury of the head. I regard the pink staining substance as the antecedent, if not the actual hormone material, therefore the above described condition of the Leydig's cells is indicative of an exhausted condition and temporary failure in their function; and associated therewith was an arrest of the final stages of spermatogenesis.

It may be hypothecated that the vital impulse of the social organism (the body) was all concentrated in an attempt to preserve the life of the individual; the formative energy of the testis being in abeyance, the vital energy of the sex instinct was available for prolonged formative cell activity of phagocytes and pus formation.

I have shown that in many fatal cases due to microbial invasion of the body, such as tuberculosis, pneumonia, broncho-pneumonia, typhoid and dysentery, active spermatogenesis in all stages can be seen in the majority of cases; in some, especially those dying within a short time of the onset of the disease, pink eosin-stained islands and islets of Leydig cells are seen. Indeed, a case of infective endocarditis, aged 21, that developed a cerebral aneurysm and died suddenly of apoplexy from its rupture, showed normal interstitial cells and normal active spermatogenesis. But as a rule the pathological changes indicating functional exhaustion of the interstitial cells are more marked when there are circulating microbial toxins from chronic diseases than can be observed in the epithelial cells of the spermatic tubes. The spermatogenic cells may be protected by the basement membrane and the abundance of lipoid cholesterin ester with which it is covered, both within and without.

THE STRUCTURE OF THE BASEMENT MEMBRANE OF THE TUBULES AND ITS RELATION TO LYMPHATICS.

The basement membrane of the tubules appears to consist of a delicate connective tissue lined externally by flat endothelial cells (*vide* figs. 1 and 2, Plate I). When the membrane undergoes thickening owing to regressive atrophy of the spermatogenic cells, these structures undergo proliferation. In a case of dementia præcox that died of chronic nephritis and in which the testes showed microscopically advanced regressive atrophy, yet owing to the œdema were nearly of normal weight (*vide* Table IV, No. 13), microscopic examination of sections of the organ showed that the thickened membrane was separated by the œdema into layers. The Sertoli cells and spermatogonia rest therefore upon a layer of connective tissue and endothelial cells, external to which is a lymph space, the external wall of which is similar to that of the basement membrane. External to this lymphatic space, and resting upon it, are the Leydig cells. These anatomical dispositions can often be clearly made out in normal tissues. Examination of frozen sections stained with scharlach and hæmatoxylin show drops and droplets of lipoid substance in this lymphatic space and in the lymphatic clefts of the interstitial tissue, also in the Leydig cells. Very fine

droplets can be seen in the Sertoli cells, and these undoubtedly serve for the growth and development of the spermatozoa.

THE ORIGIN AND DESTINATION OF THE INTERSTITIAL LIPOID.

The question arises: Does this lipid, which is seen in the interstitial lymphatics, serve as the raw material elaborated by the Leydig cells for spermatogenesis, or does it represent a waste product of spermatogenesis to be taken away by the circulation? The following arguments are in favour of the former hypothesis:—

(1) The correspondence between the disappearance of Leydig cells and cessation of spermatogenic epithelial growth.

(2) The reappearance of Leydig cells before signs of spermatogenesis.

(3) The presence of lipid in the interstitial cells.

(4) The presence of lipid in the Sertoli cells when the remaining cells have undergone complete regressive atrophy, and when this occurs interstitial cells containing lipid also exist.

(5) The interstitial cells by this hypothesis would perform a double function, viz., by a decomposition of the eosin-staining substance (corresponding to a zymogen) a hormone would escape into the circulation and the lipid would pass into the lymphatic space surrounding the tubule and thence into the Sertoli cells possibly by the active intervention of the endothelial cells.

(6) In the undescended testis, the tubuli seminiferi are inactive and undeveloped but the interstitial hormone cells persist; they contain these lipid granules, so that they retain the function of providing a sexual stimulant apart from spermatogenesis. They thus provide the mental and bodily conditions required for coitus. Not only do these cells retain their anabolic function of storage of the zymogen and production of hormone, but the presence of lipid granules in their interior shows that in the undescended testis they retain a katabolic action in their interior. In the freemartin—a bull with undescended testis—I found a non-existence of seminiferous tubules, but the gland consisted of fibrous tissue and fibroblasts, amongst which are large polygonal cells with round nuclei; many of these interstitial cells contained lipid granules stained black by osmic acid.

It is well known that cryptorchids have sexual desire, and that ligature of the vas deferens, on both sides, which causes complete obstructive atrophy of the tubules, also exposure of the testes to X-ray which destroys spermatogenic function, leave the interstitial cells intact and with their integrity the sexual appetite persists.

ANALOGY OF THE CELLS OF THE THECA INTERNA OF THE GRAAFIAN FOLLICLES AND THE CELLS OF LEYDIG.

Examination of the ripening Graafian follicles shows that the cells of the theca interna take the eosin stain and that if the section be stained with scharlach it will be found that in these cells and between them and between the cells of the zona granulosa are numbers of lipid granules.

A section of the ovary of a child aged 18 months shows the eosin-stained theca interna surrounding a Graafian follicle. Inasmuch as from early infancy onward Graafian follicles with these cells of the theca interna are continually formed, it may be presumed that they have a function. Now the somatic cells possess both male and female characters but the male are dominant; it seems therefore probable that these thecal cells are continually being formed

under the stimulus of follicle development. As they do not become mature enough to rupture but form atretic follicles, it may be assumed that this follicular formation is for the purpose of secreting a hormone to maintain the female characters in the somatic cells.

Young pullets that had had the ovaries removed developed into birds that look like cockerels and behave like cockerels. The fact that castration in early life does alter the mental and bodily characters of the individual, yet does not produce insanity, indicates that the changes in the central nervous system in dementia præcox are not dependent upon the regressive atrophy of either the interstitial or the spermatogenic structures, but that dementia præcox and dementia presenilis constitute an innate germinal defect which is manifested obviously in the two tissues of the body essential for the preservation of the species, viz., the brain, the organ of external relation and the reproductive organs.

THE VITAL IMPULSE.

There is an inherent lack of durability or vital energy in the neurones, especially those latest developed ontogenetically and phylogenetically. But this lack of vitality in dementia præcox is probably not confined to these two tissues; being of biogenetic origin it affects sooner or later all the active functioning tissues of the body and there is a corresponding deficiency in oxidation processes.

I do not recollect having seen a case of dementia præcox in a congenital syphilitic, nor have I observed a positive Wassermann reaction in the blood or fluid of cases of dementia præcox, although a great number have been examined. There is no reason why a case of congenital syphilis should not develop symptoms of dementia præcox. Indeed, I have seen a case of juvenile general paralysis with symptoms of hebephrenia. I have occasionally seen cases of dementia præcox diagnosed general paralysis on account of delusions of grandeur, but they gave negative Wassermann reactions and at death no naked-eye or microscopic signs of general paralysis were found. I have not found any evidence to correlate any intimate connexion between this disease and syphilis or alcoholism in the parents.

The reason for the absence of acquired syphilis in dementia præcox cases is that the male is not as a rule attracted to the opposite sex, indeed feeling his inadequacy he usually rather shuns and avoids females.

THE SEXUAL FUNCTION AND AUTO-INTOXICATION.

It has long been thought, and it has been taught by Kräpelin, Urstein and other authorities, that an intoxication arising from a disturbance of the normal functions of the sexual glands is an essential pathological condition in dementia præcox. If there be an auto-intoxication by disorder of the sexual functions is it direct or indirect in its effects upon the functions of the brain?

An excess or deficiency of the sexual hormone may certainly cause a disturbance of the normal biochemical equilibrium of the endocrine gland function, sufficient to make a latent potential psychotic individual actively anti-social, and thus reveal the mental disease.

If it be granted that the psycho-physical energy of the sex instinct is activated by hormones secreted by the interstitial cells a deficiency would be associated with a depression of psycho-physical energy and the mental disorder would be revealed.

Now there is in dementia præcox usually a simultaneous regressive atrophy

of both the interstitial cells and the spermatogenic cells of a progressive character; moreover, as a rule, there is a correspondence in the intensity and degree of the atrophy of these two essential structures in the male organ of reproduction (*vide* Table I). It will therefore be interesting to study the male reproductive organs (1) in extreme old age; (2) in general paralysis of the insane; (3) in post-adolescent psychoses; (4) in dementia præcox.

The Testes in Octogenarians.

I have examined the testes of three octogenarians suffering with senile dementia, aged respectively, 81, 83, and 86. In the old man of 81 there was active spermatogenesis. The testes were of average normal weight and presented a fairly normal macroscopic appearance; beyond some atrophy of the tubules and thickening of the basement membrane, the tubes and the spermatozoa found in the tubules were for the most part normal as regards the staining reactions. There was certainly, as compared with a young normal adult, a diminished spermatogenic activity and a very considerable diminution in number of the interstitial cells. Small islands and islets of pink eosin-stained cells could be discerned with a low power, and examined with an oil immersion these cells presented a fairly normal appearance with the exception that many of them were pigmented (*vide* fig. 1, Plate IV). The sections presented less evidences of deficiency of functional activity than did the great majority of the cases of dementia præcox, and of several of the cases of presenile atrophy occurring in males at an age between 50 and 60, who presented signs and symptoms of dementia præcox (*vide* fig. 3, Plate I), or in cases of involutional melancholia.

The other two cases, aged 83 and 86, showed a much more advanced failure of spermatogenic function, and the tubules exhibited a marked regressive atrophy in many respects corresponding to the third stage of regressive atrophy of dementia præcox. Excepting in the following facts that many of the tubes showed heterotypical mitosis and here and there a few spermatozoa, the chromatin of the nuclei presented a normal staining reaction; here and there small islands of normal stained, but pigmented, Leydig cells could be seen in the interstitial tissue.

The pigment in the cells, it may be presumed, is evidence of senility; but we shall find that in a large proportion of the cases of dementia præcox occurring in young adults dying under the age of 30 and in the presenile cases (*vide* Table IV), pigmented cells are present (*vide* fig. 4, Plate I), and in one case of dementia præcox who lived fifteen years after the onset of symptoms the great majority of the interstitial cells that still remained were pigmented (*vide* No. 27, Table I).

Having thus established the fact that the hormone cells persist to a very old age, which accords with the known fact of persistent sexual desire, it follows that if in young adults we have a condition in many ways similar to this senile change, it may be regarded as probable that there is a germinal precocious senility, and therefore of formative capacity of the reproductive organs in dementia præcox, which, arising at puberty or early adolescence in the great majority of cases, progresses and finally leads to a complete loss of reproductive power.

The Testes in General Paralysis.

The average weights of the testes after removal of the epididymis and tunica albuginea of twenty-four cases of general paralysis were 16.5 and 16.9 grm., or together 33.4 grm.

The average weights of the testes after removal of the epididymis and tunica vaginalis in twenty-seven cases of dementia præcox were respectively 12.5 and 13 gm., together 25.5 gm. (Table I).

The average weight therefore of the testes in dementia præcox is nearly 8 gm. less than in general paralysis.

Examination of an emulsion of the testis in cases of general paralysis by dark ground illumination in the twenty-four cases, with very few exceptions, showed spermatozoa, whereas in the twenty-seven cases of dementia præcox quite two-thirds showed no spermatozoa.

I have examined microscopically the testes in twelve cases of general paralysis unselected. The average age at death of these twelve cases was 49.5. The youngest was 28 and the eldest 58. The heaviest pair of testes was 30 gm. each (age 46) and the lightest pair was 11.5 gm. and 12 gm. respectively. There were five of the twelve cases which upon microscopic examination showed generalized active spermatogenesis in the tubules and fairly normal interstitial cells and lipoid; the average weight of the pair of testes in these cases was 44 gm. and the average age at death was 38. Of the remaining seven of which microscopic examination was made, it was observed that in most cases there was normal active spermatogenesis taking place in some of the tubes, but scattered about in the organ were strands and areas of completely atrophied tubules without cells of Sertoli. Often one testis would show this more markedly than the other, and not infrequently there were naked-eye appearances of old inflammatory conditions such as adhesions of the tunica vaginalis and one with melon seeds. These areas of atrophy were either due to a local specific inflammatory condition or probably more often to a gonorrhœal epididymitis with secondary atrophy from obstruction of the vasa efferentia. In these latter cases amidst the atrophied tubes or more often in the neighbourhood were visible under a low power islands and islets of eosin-stained Leydig cells. It may be remarked that in most of the cases, especially those whose age was over 40, the interstitial cells contained pigment. In only one of these twelve cases could I not see under a low power some evidence of eosin-stained clumps of Leydig cells. In most of the cases they were less numerous than in the normal man of a similar age, but this may be due to the fact that in the majority of cases death occurred in or past the prime of life and many had suffered from an intercurrent, often chronic, disease which would tend to exhaust the Leydig cells and arrest spermatogenesis. Yet comparatively to the cases of dementia præcox (*vide* Table I) and the post-adolescent cases presenile (*vide* Tables III and IV) the difference was striking. I have only once found absolutely complete arrest of spermatogenesis in this disease, and that was in a case of prolonged seizures (status), inanition and exhaustion. Even in testes weighing less than 12 gm., evidence of considerable atrophy, I have found some of the tubules showing active heterotypical mitosis and spermatogenesis. Moreover, the nuclei and the mitotic figures showed a good basophil reaction, contrasting in this respect to the tubules in the earlier stages of dementia præcox where as often as not I found unequal basophil nuclear staining.

The Testes in Post-Adolescent Psychoses.

In Tables III and IV there are thirteen cases of post-adolescent psychoses. If we analyse these Tables we see that in a case of Korsakoff psychosis (No. 5) dying at the age of 55 the testes weighed 14 gm. each; there was a recent arrest of spermatogenesis which I associated with a carcinomatosis of the cirrhotic

liver and paracentesis; it will be noted, however, that Leydig cells were visible with a low power, and pigmentation was not observed. The cases of manic-depressive insanity, in which there was no terminal dementia, exhibited active spermatogenesis but the interstitial cells were relatively deficient. In the cases where the manic-depressive condition terminated in dementia and in the cases in which symptoms like those of dementia præcox—cases which it may be permissible to call dementia presenilis—occurred, the testes were greatly diminished in weight and exhibited appearances similar to those observed in advanced dementia præcox (*vide* Cases, Tables III and IV, and fig. 3, Plate I).

The investigations are not sufficiently advanced to do more than conjecture that the manic-depressive state may possibly be related to the deficiency in the formative activity of the Leydig cells and the influence of such deficiency on the endocrine system. The close relation of manic-depressive insanity to dementia præcox is shown by the fact it may end in a terminal dementia and the microscopic appearances of regressive atrophy of the testes in such cases resemble those met with in dementia præcox. It would be interesting to examine the brains in these cases for I expect we should find similar histological changes also.

THE MORBID CHANGES OF THE TESTES IN DEMENTIA PRÆCOX.

I will now analyse the findings in the twenty-seven cases of dementia præcox contained in Table I. It may be mentioned that in the majority of the cases sections of frozen tissues were stained with scharlach and hæmatoxylin-eosin. Lastly, to prevent shrinkage, blocks of the tissues were embedded in celloidin, taken out and allowed to skin over, then placed in chloroform and subsequently embedded in paraffin and cut in serial sections; in this way shrinking was prevented and the cells were thus prevented from dropping out.

SUMMARY OF THE RESULTS OF THE MICROSCOPIC EXAMINATION OF THE TESTES IN DEMENTIA PRÆCOX.

The results of the microscopic examination of the twenty-seven cases of dementia præcox are summarized in tabular form. In a previous publication in which I devoted special attention to the condition of the spermatogenic tubules in twenty-three cases, I divided the cases into three classes or stages of regressive atrophy of the spermatogenic cells.¹ In the first stage I included those in which the changes could be discovered by comparison with the normal. Active spermatogenesis could be observed in numbers of tubules, but examination with an oil immersion lens showed that the heads of the spermatozoa were not infrequently of irregular shape, unequal size and staining with eosin instead of the basic dye. There was one case, No. 6 (*vide* fig. 4, and fig. 2, Plate II, Part II).

The second stage I have divided into early and late: Nos. 8 and 11, early stage. In these there were many tubules showing active spermatogenesis, but many in which there was very obvious regressive atrophy of the spermatogenic cells and thickening of basement membrane. There were pronounced changes of the Leydig cells in both (*vide* fig. 2, Plate IV, Part II).

The Second Stage.—More pronounced spermatogenic regressive atrophy of tubules, thickened basement membrane, Nos. 1, 4, 5, 7, 12, 14, 18, 23, 27, but still some tubules show spermatozoa. No eosin clumps of Leydig cells seen with low power (fig. 4, Plate IV, Part II).

¹ Figs. 4 and 5, Plate II, Part II.

The Third Stage.—No spermatogenesis, tubules atrophied, often containing only Sertoli cells, with lipoid granules, thickened basement membrane. No normal Leydig cells—generally increase of fibroblasts (figs. 5 and 6, Plate II, Part II).

There is a general correspondence in the amount of regressive atrophy of the interstitial cells and the spermatogenic epithelium. In the normal, and in certain forms of mental disease, especially general paralysis, epilepsy, senile dementia, organic dementia, Korsakoff psychosis and some cases of manic-depressive insanity without dementia, the interstitial cells can be seen as eosin-stained clumps with a low power (*vide* figs. 1 and 3, Plate IV). This occurred in only two cases, in which the patients had only been eighteen months in the asylum (*vide* fig. 2, Plate I). As I have mentioned that in prolonged and extensive suppuration occurring in hospital cases the eosin substance disappears, it might be said that the absence of clumps of eosin-stained cells visible with a low power was due to the intercurrent disease, especially pulmonary tuberculosis, which accounted for death in seven of the twenty-seven cases. But four of the number died of acute lobar pneumonia after a few days' illness and some from acute or subacute dysentery, and the normal Leydig cells were not visible in all but two of these, presumably early cases (4 and 6, Table I). Moreover, in general paralysis and other psychoses or brain disease, the intercurrent disease did not cause a disappearance of the eosin-stained clumps of cells. It may, therefore, be presumed that in dementia præcox there is a regressive atrophy and failure of function of the interstitial cells coincident with, and in great measure proportional to, the regressive atrophy of the spermatogenic epithelium. With this regressive atrophy is a diminution and in a few cases an almost total disappearance of the interstitial lipoid.

The pathological changes thus appear to affect the functions of the interstitial cells and the spermatogenic epithelial cells. In some few cases, especially in the cases of psychoses, death occurring in the post-adolescent stages of life, the two tissues are not equally affected. In the manic-depressive type several cases showed fairly normal spermatogenesis and a marked diminution of normal interstitial cells. Again, in a case of chronic Korsakoff psychosis with cirrhosis of liver and carcinomatosis, the spermatogenic tubules showed no spermatogenesis but fairly normal interstitial cells. A glance at Mr. Kenneth Walker's cases of men dying late in life, shows that sometimes the degree of regressive atrophy of the two tissues do not appear to coincide (*vide* Table II, p. 24). Of course, allowance must be made for the fact that this is not conclusive evidence, for one part of the testis may show active spermatogenesis, another not; and again, one part may show normal interstitial cells, another not.

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PHOTOMICROGRAPHS.

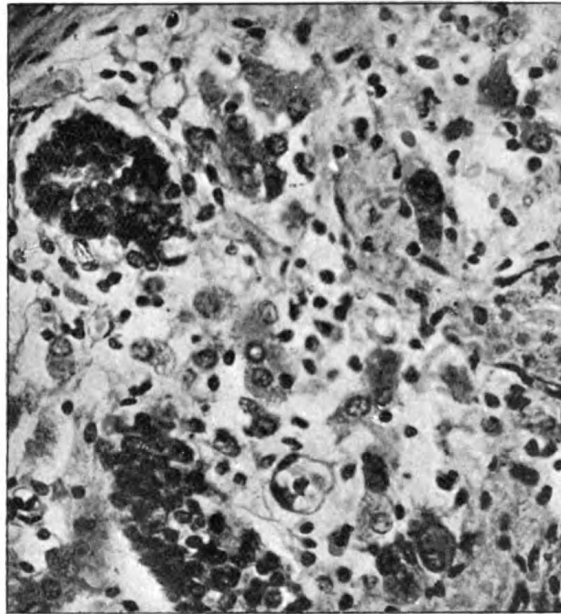


FIG. 1.

(1) Section of testis of new-born child. Showing embryonic tubules and polygonal mature interstitial cells with round nuclei. Many small immature cells are present but not so distinctly seen lying in loose areolar tissue. (Staining hæmatoxylin-eosin. Magnification 410.)

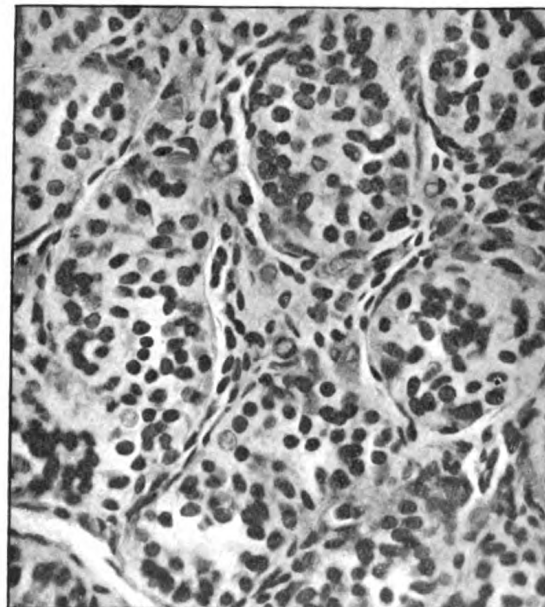


FIG. 2.

(2) Section of testis of child, aged 4 months. The tubules are nearly double the size and approximated; here and there are small areas containing a few small faint pink polygonal cells, but for the most part the normal interstitial cells have disappeared. The portion of the section in the centre containing the residue of the interstitial cells was found after search. (Staining hæmatoxylin-eosin. Magnification 430.)

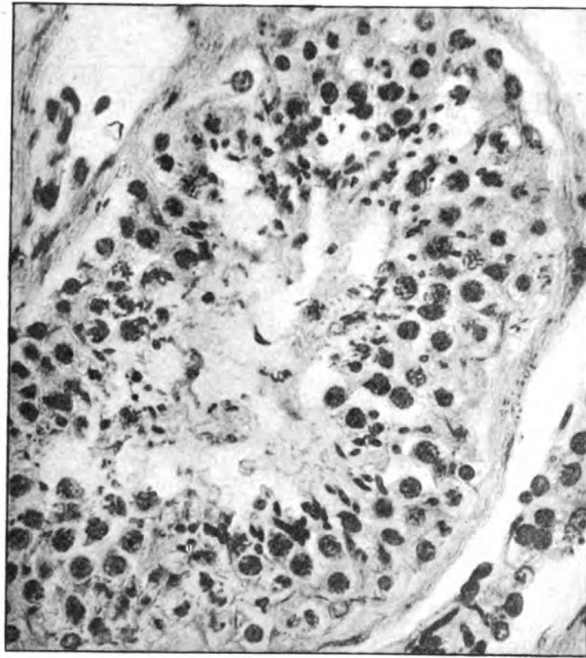


FIG. 3.

(3) Section of testis, Case 6, Table I. Low power, showing tubule with active spermatogenesis. In some places the spermatozoa are normal in appearance and staining reaction; in others they are of unequal size and abnormal form and staining. (Staining Heidenhain-hæmatoxylin. Magnification 500.)



FIG. 4.

(4) High power (oil immersion) of the same section, showing a group of these degenerated spermatozoa. Observe the heads of the spermatozoa are of unequal size and shape, and do not take the nuclear stain, although the chromatin in the adjacent cells is well stained. (Magnification 1,200.)

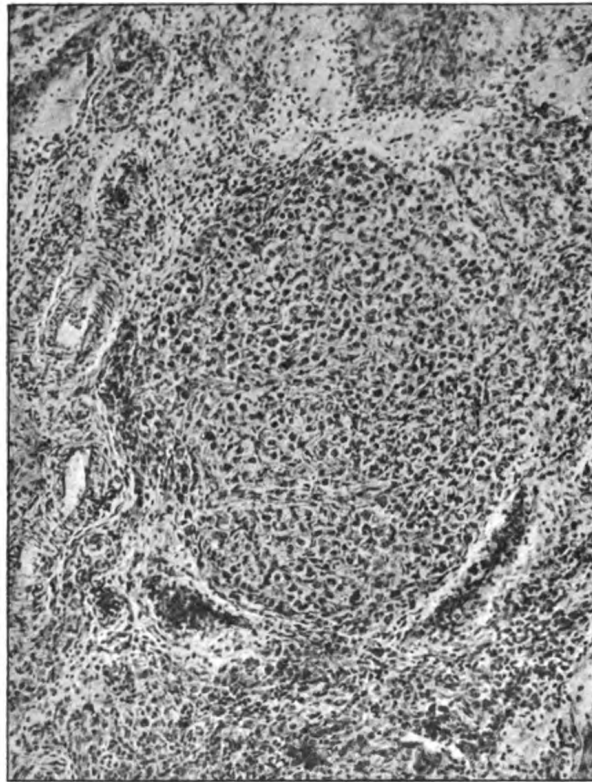


FIG. 5.

(5) Section of testis. Nodule of interstitial cells. Case 25, Table II. Extreme atrophy of tubuli seminiferi. The interstitial cells form a nucleated syncytium. Some contain lipoid substance, and the cytoplasm does not stain with eosin. (Magnification 120.)

EXPLANATION OF PLATE I.

FIG. 1.—Section of testis from a case of death from shock due to severe injuries. A number of interstitial cells are seen of varying size. The eosin-stained cytoplasm is vacuolated. The nuclei are well stained by the basophil dye, and show in two of the cells active mitosis.

FIG. 2.—Section of testis from Case 6, Table II. Many interstitial cells are seen around a small vessel. They are not so numerous as in fig. 1, and there is a vacuolated syncytium in the lower part of the figure. The flattened cells of the basement membrane are increased.

FIG. 3.—Section of testis of dementia præcox advanced second stage. A small vessel in centre. Above thickened basement membrane with flattened nuclei a few small immature Leydig cells are seen. A few large with vacuoles. A large number of oval and polymorphic pale nuclei, some of which are fibroblastic, are seen. Compare with figs. 1 and 2. The appearances are similar to the regressive atrophy of the interstitial cells seen in photomicrograph fig. 3 of the infant's testis at 4 months.

FIG. 4.—Section of testis of primary post-adolescent dementia, Table IV, Case 10. Nearly all the interstitial cells are markedly pigmented. The nuclei are large, oval and pale, indicative of a deficiency of chromatin.

All the specimens were stained with hæmatoxylin eosin, and the magnification one-twelfth oil immersion, and No. 4 ocular Zeiss.

PART II.

The Morbid Histology of the Testes in *Dementia Præcox*.

By MIGUEL PRADOS Y SUCH, M.D. Madrid.

SIR FREDERICK MOTT has placed at my disposal the testes of a number of his cases, and I have examined sections which I have prepared by the Del Rio-Hortega silver method, which is especially useful for demonstrating the spermatozoa and nuclear changes. I have also examined a number of his sections of testes stained by hæmatoxylin-eosin with a view of showing the changes in the interstitial cells in dementia præcox and other diseases when compared with the normal. My findings agree with the description which he has given in Part I. But before proceeding to describe the results obtained by my investigations I will describe the Del Rio-Hortega method, which I generally used. Of the various modifications of this method the following was the one generally used by me, as the tissues had been hardened in formol:—

NUCLEAR STAINING.

Sections cut by the freezing method are taken from distilled water, placed into the silver solution (*see below*), and warmed at a temperature of 50° to 55° C. until slightly yellow in colour. They were then placed direct into a 2 per cent. solution of formol (neutralized by calcium carbonate) until the section becomes black. Washed in distilled water for about one minute and then placed into gold chloride solution (1 in 500) until the section becomes grey, usually about half a minute. Then into a 5 per cent. solution of hyposulphite of soda for five minutes: in this it becomes a rose colour. Wash in water, fix section to slide, blot off excess of water, and dehydrate with a creosote-carbolic-xylol mixture (creosote, 10 c.c.; carbolic acid, 10 grm.; xylol, 60 c.c.), and mount in Canada balsam.

Silver Solution.—5 c.c. of a 10 per cent. solution of aq. No. 31, precipitated by 20 c.c. of a 5 per cent. solution of carbonate of sodium; dissolve precipitate by few drops of ammonia, and add water to 55 c.c.

PLATE I.



FIG. 2.

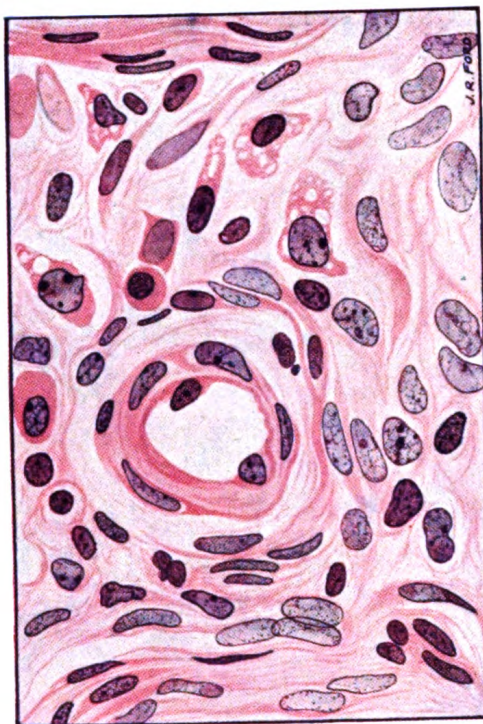


FIG. 3.



FIG. 1.

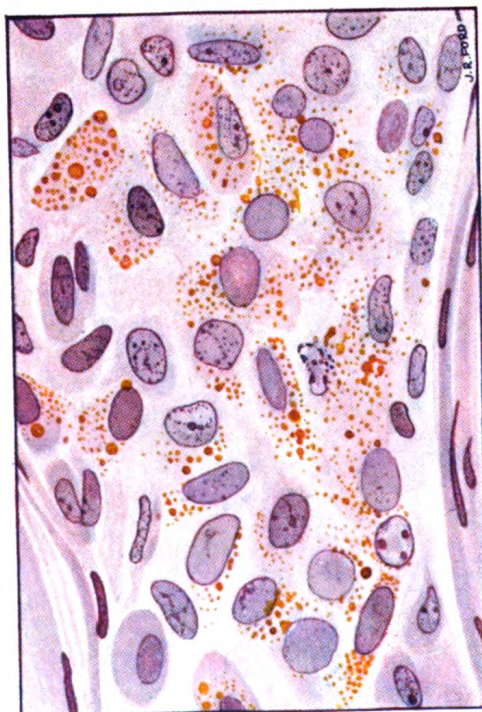


FIG. 4.

MOTT and SUCH:
Further Pathological Studies in Dementia Præcox.

SPERMATOGENESIS.

I have examined sections of a series of testes from the following cases and Plates II, III and IV with the descriptions summarize the histological changes I have observed.

(1) Normal, in which death resulted from shock caused by severe injuries (fig. 1, Plate II). It will be observed that the heads of the spermatozoa are uniformly stained and uniform in size and the spermatocytes all show nuclear skeins; there is no thickening of the basement membrane.

(2) Section of testis of No. 6, Table I, Part I. Section of the tubule in which the earliest changes can be observed. In many of the tubules these changes would not be found. Compared with the normal many of the heads of the spermatozoa are imperfectly stained, they are not of uniform shape and size; the tails are imperfectly formed and fewer spermatocytes show the nuclear skein; the basement membrane shows some thickening (*vide* fig. 2, Plate II). This change in the spermatozoa was observed also by the hæmatoxylin-eosin method of staining (*vide* photomicrograph, fig. 4).

(3) Section of testis of No. 8, Table I. Section of a tubule in which early changes can be observed in the spermatozoa similar to the previous one but rather more marked (*vide* fig. 3, Plate II). It will be observed that the testes in both these cases were of fair weight and the duration of time in asylum was under two years and showed first stage of regressive atrophy.

(4) Section of testis of No. 5, Table I, second stage of regressive atrophy. Some few tubules showed spermatogenesis but the great majority showed absence of spermatogenesis; formation of spermatids were found in some tubules, in others no heterotypical mitosis (*vide* fig. 4, Plate II).

(5) Section of testis of No. 15, Table I, third stage of regressive atrophy; no spermatozoa; no evidence of heterotypical mitosis, great thickening of basement membrane and overgrowth of fibroblasts (*vide* fig. 5, Plate II).

(6) Section of testes of No. 12, Table I, third stage of regressive atrophy. Great deficiency of nuclear stainable substance, absence of heterotypical mitosis, great increase of interstitial tissue and thickening of basement membrane (*vide* fig. 6, Plate II).

It will be observed by reference to the table that in these cases the weights of the testes correspond fairly well to the three stages of regressive atrophy of the organs. The results in the main confirm the findings obtained by Sir Frederick Mott by the methods he employed.

INTERSTITIAL TISSUE.

Examination of the interstitial tissue by the Del Rio-Hortega method. The normal case showed the following appearances. Single polyhedral cells with cytoplasm fairly deeply stained containing a round nucleus with deep chromatin staining and three crystals in the cell. A less well stained syncytium with six nuclei, each having a fairly well stained chromatin network. Within the syncytium of cells are seven varied sized crystals (*vide* E, Plate III). These were not seen in the pathological condition of the testis.

Section of testis No. 5, Table I, shows a syncytium of cells with fibrous tissue between and two nuclei of fibroblasts. The nuclei are pale and, excepting the nucleolus which is not observable in the normal interstitial cells, hardly take the stain. The cytoplasm is faintly stained in parts of the cells (*vide* F, Plate III).

Section of testis of No. 15, Table I, shows a number of cells separated by fibrous tissue and fibroblasts. The nuclei are very pale excepting the nucleolus: the cytoplasm is unstained (*vide* G, Plate III).

PLATE II.

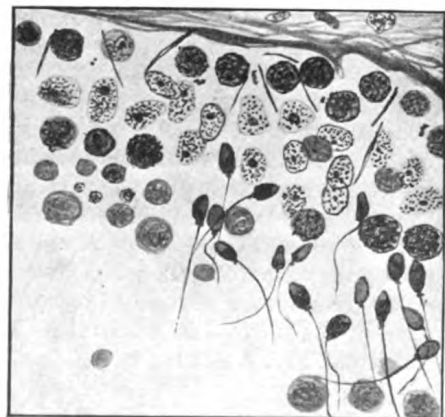


FIG. 1.

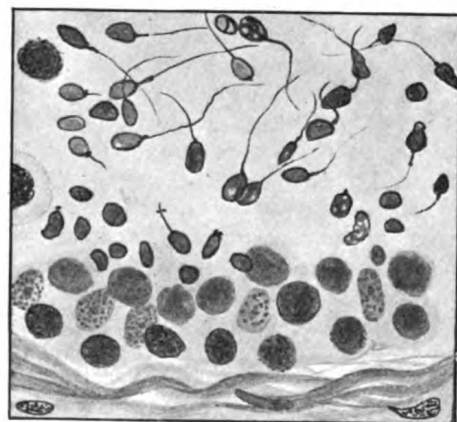


FIG. 2.

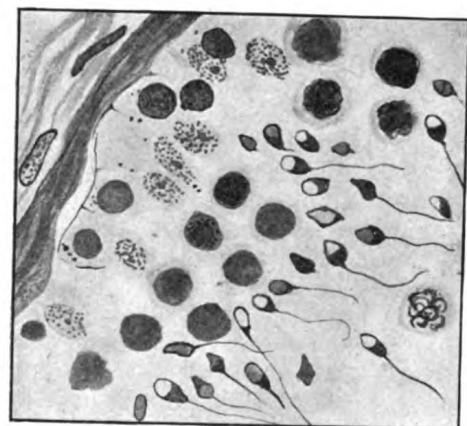


FIG. 3.

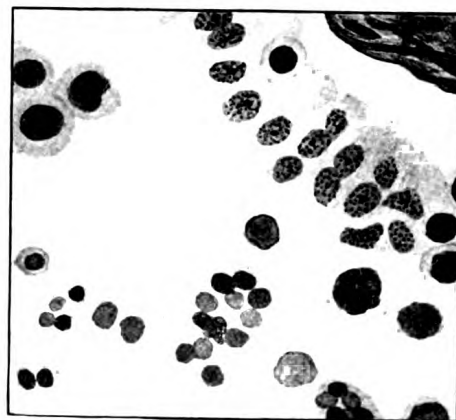


FIG. 4.

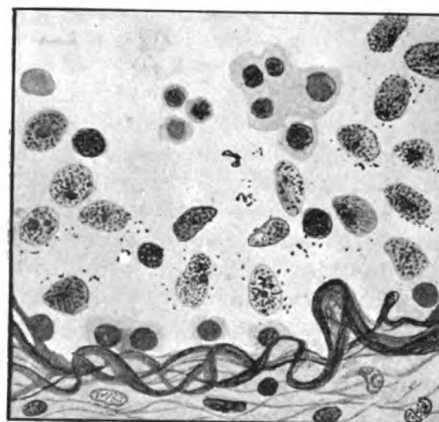


FIG. 5.

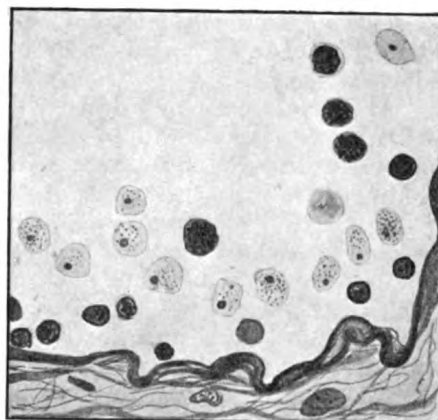
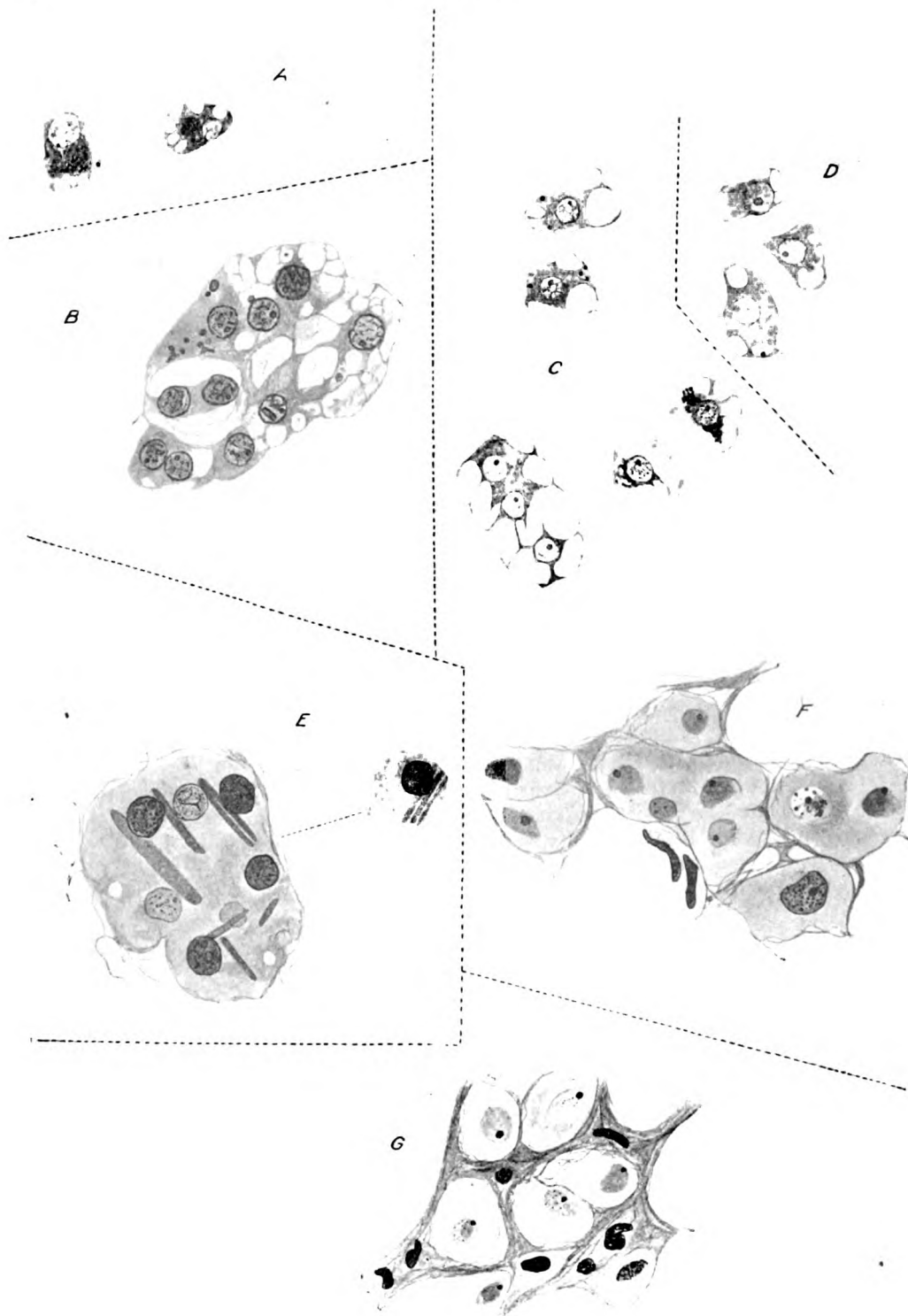


FIG. 6.

PLATE III.



INTERSTITIAL CELLS STAINED BY DEL RIO-HORTEGA METHOD (PLATE III).

Two pigmented cells: A, Plate III, showing a mass of pigment occupying the greater part of the vacuolated cells. The nucleus is very pale and contains very little chromatin (Case 7, Table I).

A group of vacuolated interstitial cells, B, Plate III, showing nearly normal staining nuclei, some pigment granules (Case 14, Table I).

Three sets of vacuolated cells, one forming a syncytium by the vacuolation: C, Plate II, nuclei round but paler than normal; the other pairs of cells show pigment granules in the cytoplasm (Case 9, Table I).

Three cells from a surgical case, D, Plate III, showing vacuoles at the periphery of the cell, no pigmentation although obtained from a man in the prime of life.

Magnification oil immersion lens and No. 4 ocular.

INTERSTITIAL CELLS.

Examination of Hæmatoxylin-eosin Preparations.

(1) Section of testes of a man, aged 81, suffering with senile dementia referred to in Part I. On the left a portion of tubule is shown exhibiting spermatogenesis with normal stained heads of spermatozoa, the basement membrane of this tubule and the adjacent one, which shows normal staining spermatogonia and spermatocytes, is thickened by an increase of fibroblasts. Above is an isolated small interstitial cell and above this a group forming a syncytium by vacuolation, the nuclei of normal shape and staining; one cell contains pigment granules (*vide* fig. 1, Plate IV).

(2) Section of testis of normal case dying of shock described in Part I showing abundance of normal interstitial cells lying between the tubules. They are most of them mature and contain a good amount of eosin staining substance although the vacuolation would show that for the most part they contained lipoid. There are three young cells lying together showing no vacuolation (*vide* fig. 2, Plate IV).

(3) Section of testis of a case of juvenile tabo-paralysis. Spermatozoa were found in the vesiculæ living eight hours after death. Most of the tubules showed normal active spermatogenesis. There was some thickening of basement membrane of tubules; this is seen in the tubule on the right by the increase of fibroblast nuclei. There are abundant normal interstitial cells which are visible as eosin-stained clumps with a low power. The nuclei are well stained and there are no fibroblast nuclei intervening (*vide* fig. 3, Plate IV). This should be compared with the next figure (4).

(4) Section of testis from Case 19, Table I. Observe the great fibroblast nuclear proliferation of the basement membrane upon which lies only a syncytium of Sertoli cells. The interstitial tissue consists of a very vacuolated syncytium of cells with pale nuclei of irregular form and size. The elongated more deeply stained nuclei are the nuclei of intervening fibroblasts (*vide* fig. 4, Plate IV).

SUMMARY OF THE LITERATURE OF THE INTERSTITIAL CELL.

The Interstitial Cell.

The interstitial cell consists of a more or less eccentrically placed mass of condensed granular cytoplasm containing a nucleus; the peripheral portion of the cell may however be extensively vacuolated. Von Lenhossek has in con-

PLATE IV.

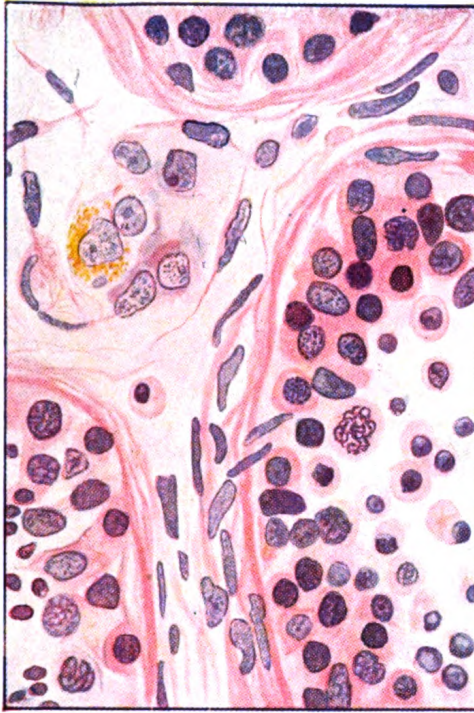


FIG. 1.



FIG. 3.



FIG. 2.

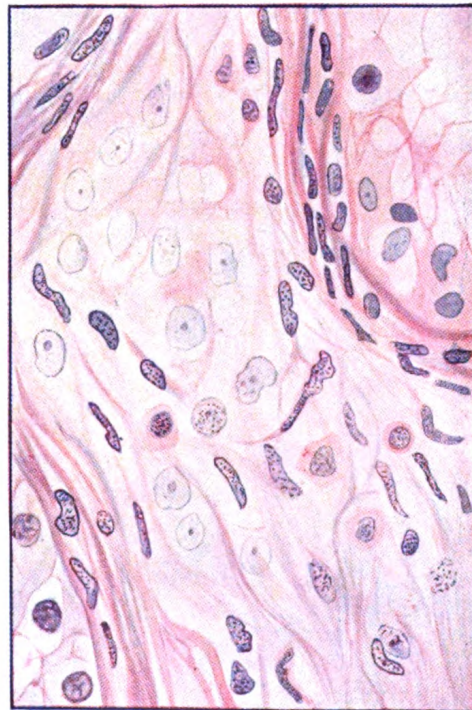


FIG. 4.

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sequence applied the terms "endoplasm" and "ectoplasm." This typical structure is not found in all the cells but all gradations may be observed from cells whose bodies are composed entirely of "endoplasm" to those in which it is reduced to a remnant in the immediate vicinity of the nucleus. Plato regards these vacuolated forms as old cells, the opposite extreme being youthful forms; however their presence is restricted to a very few animals, if indeed it is not limited to man. They were found by Ganfini only in man. Whitehead, in a long series of mammals, also found them only in man. Nothing is known about their chemical composition and their inconstancy gives them little importance. But it has been pointed out in Part I that there is a correspondence of vacuolation and lipid in the cells.

Specific Granules.—Regand describes certain secretory vesicles in the rats' testicles fixed in Tellyesniczky's fluid (equal parts of 3 per cent. sol. potassium bichromate and 5 per cent. acetic acid). With many methyl blue-eosins they stain red; they are brought up well by iron hæmatoxylin, although the best is the Reinke's neutral gentian as modified by Dersley. In such preparations the majority of the interstitial cells contain definite granules, one or two microns in diameter, often in clusters. They lie for the most part in the peripheral portion of the cells but may be found anywhere in the cytoplasm. Each granule is contained in a distinct vacuole (thin sections). In the case of cells which contain many fat globules they and their granules must lie in the same vacuoles.

The staining reactions of these granules and their resistancy to acetic acid call to mind the zymogen granules of the pancreas. On the other hand, the reaction for prozymogen, which usually can be obtained in cells which produce zymogen, could not be obtained. But, without any reference to their chemical nature, we may regard the granules as an internal secretion of the interstitial cells.

The interstitial cells appear long before the epithelium of the tubules have become active.

Addison Thornton states that vital staining with trypan blue reveals two types of cells in the internal structure of the testis. One is elongated in the form of fibroblast, while the other is rounded or polyhedral in shape. Both types, according to the definition of Evans, are to be considered as macrophages and are not, as Goldmann interpreted them to be, identical with the interstitial cells of Leydig which represent the testicular organ of internal secretion. The vital staining with counterstain make it possible to differentiate between the interstitial cells and the macrophages.

Pigment.—"This is not present in any of my material (man, cat, opossum, pig, rabbit, dog, sheep, bull, grey squirrel and rat) and accordingly is not a constant content of the interstitial cells." Sebrt, who has made the latest study of its nature, finds that it is fatty, staining well with Sudan III in frozen sections and faintly even in material that has been treated with alcohol. He considers it to be a waste pigment.

Crystalloids.—The discovery by Reinke in 1896 of crystalloids in the interstitial cells of an executed criminal aroused considerable interest at first and his findings were confirmed by Lenhossek and others. It soon became evident, however, that their presence is restricted to a very few animals, if, indeed it is not limited to man; they were found by Ganfini and by myself only in man. I shall content myself with simply noting their inconstancy.

Function.—Plato held that it was the function of the interstitial cells to act as nurse cells, passing their fat and pigment through minute canals in the

walls of the tubules to be received by the Sertoli cells and there used as pabulum in the formation of spermatozoa. His theory was supported in some measure by Friedman and von Lenhossek but no one has been able to confirm his statements as to the existence of canals in the walls of the tubules and the passage of fat through them. Indeed the presence of fat in the lymphatics of the testicle would indicate that the flow of fat is away from the tubules, while Ganfini thinks that this appearance is a secretory phenomenon unconnected with the production of fat. The analogy with what has been observed in various gland cells is certainly very suggestive of secretory function, but probably the activity of the cells is not limited to the formation of fat. It should be stated that the vacuoles are not always so smooth and regularly circular; frequently they are large, irregularly shaped cavities with more or less ragged margins, doubtless the result of the breaking down of the partitions between adjacent vacuoles. It is hardly necessary to add that the demonstration of the structure of the interstitial cells require fresh tissue and good fixation. Moreover the study of the development of the interstitial cells in different animals has shown us that frequently fat is present in the tubular epithelium before it appears in the interstitial cells and that in the pigmented cells it is never present in any but the minutest amount. Finally, as Ganfini has pointed out, in undescended testes, where the Leydig cells are usually typically developed and numerous, the tubular epithelium is undeveloped or atrophied and subsequently no spermatozoa are formed.

Ganfini believes that the fat itself is the internal secretion of the cells and is poured into the general circulation through the lymphatics. He bases his opinion upon the fact that fat is found in the lymphatics leaving the testis and that the fat in the cells is in the form of more or less discrete droplets rather than in large drops as in the ordinary adipose cells and consequently is no ordinary fat.

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SUMMARY OF INVESTIGATION OF VITAMINES AND THEIR RELATION TO INTERSTITIAL CELLS.

Ezra Allen: "Degeneration in the Albino Rat Testis due to a Diet deficient in the Water-soluble Vitamine, with a Comparison of Similar Degeneration in Rats differently treated, and a Consideration of the Sertoli Cells," *Anat. Record*, 1919, xvi, p. 93.

(1) Reduction in the quantity of water-soluble vitamine in the diet of rats results in total degeneration of all the germ cells, but does not interfere with growth and development in other respects; the Sertoli cells persist.

(2) In the male this atrophy of germ cells is accompanied by hypertrophy of the interstitial tissue.

(3) The type of degeneration in the male germ cells is similar to that produced by X-ray treatment of the testis directly.

(4) A similar degeneration of the germ cells has been observed in a group of rats, part of which were subjected to prolonged alcoholization. The degeneration was found to a less extent in all but one of their five brothers not alcoholized. In this group hypertrophy of the interstitial tissue was not observed.

(5) Examination of this degenerated tissue and more careful study of normal, well-fixed tissue, confirms Regand's conclusions that the Sertoli cells form a syncytium.

(6) The nucleolus of the Sertoli cells under these degenerated conditions appears to be an equally bipartite instead of, as normally, an unequally bipartite body.

(7) The interstitial tissue is much increased in quantity in the rats put upon a reduced water-soluble vitamine."

McCarrison, "Studies in Deficiency Disease," 1921, p. 139 :—

"One of the most remarkable results of foods deficient in vitamines is the constant and very pronounced atrophy of the testicles. It occurs in extreme degree, whether the dietary is exclusively composed of autoclaved rice or whether butter and onions are added; in the latter circumstances the atrophy is slightly less extreme. It appears then to be one of the most specific of the effects of avitaminosis in pigeons. . . . Histological examination shows a complete cessation of the function of spermatogenesis. The capsule of the organ and the intertubular trabeculae are greatly thickened; the diameter of the tubules is lessened; spermatozoa, spermatids, and spermatocytes are wholly absent. The tubules are lined by a single but often incomplete layer of cells which still preserve, in a considerable proportion of their numbers, nuclei which, from their appearance and staining reactions, seem capable of regeneration."

Houlbert, *Paris Médical*, December, 1913 :—

"*Vitamine and Growth.*

"*Experiments in chickens* showed that when they were deprived of vitamines in their food the birds showed an arrest of growth and of the development of the secondary sexual characters (spurs, comb and tail feathers), and progressive anæmia. One bird killed on the fourteenth day, and on post-mortem examination was found to be in a state of extreme inanition. All organs appeared normal except the testes, which were very small, and on histological examination showed an arrest of the cellular divisions and metamorphoses which normally occurs in the seminal tubules. The interstitial cells of the testes showed a very pronounced infiltration of pigment, which as Bouin and Ancel have shown, occurs in the interstitial cells of glands whose endocrine glands are in decline. Sections of the suprarenals show an arrest of development of the chromatin cells."

SUMMARY BY SIR F. W. MOTT AND DR. PRADOS Y SUCH.

The general conclusions arrived at from the investigations contained in Part I and Part II are as follow:—

(1) The interstitial cells prior to birth act as sexual determinants, and at birth form the greater part of the interstitial tissue which constitutes the major part of the testes (*vide* fig. 1). They contain lipoid granules. Moreover fine lipoid granules are seen between the embryonic epithelial cells of the tubules.

(2) The interstitial cells after birth undergo a regressive atrophy and disappear; inasmuch as the seminiferous tubules at four months are twice the size of those at birth and are approximated, it follows that the fine lipoid granules which are found between the epithelial cells, have, in all probability, served as a pabulum for their formative activity. But since there is still lipoid in the residual interstitial cells (*vide* fig. 2), this correlation of function of the interstitial cells and the epithelial formative activity has not ceased, and it is reasonable to assume that had the child been 6 months old at death, it would have ceased and no lipoid would have been found anywhere and the following facts support this conclusion. At 10 years the tubuli seminiferi are for the most part approximated and as a rule are only a little larger than those at 4 months; there is no lipoid in the interstitial tissue, or in the tubules. There are occasionally to be seen mitotic figures as if spermatocytes were commencing to be formed, but no Sertoli cells are observable. In the interstitial tissue are seen numbers of oval, round and polymorphic nuclei, not nuclei of fibroblasts, and occasionally a definite small polygonal cell, eosin stained, can be seen, indicating that *pari passu* with the tubular epithelial formative activity there is a reappearance of the interstitial cells.

(3) The appearances of these immature interstitial cells resemble in many respects the appearances presented by the interstitial cells in advanced cases of dementia præcox (*vide* fig. 3, Plate I).

(4) At puberty and adolescence the tubules have increased in size owing to active proliferation and spermatogenesis. Abundance of mature interstitial cells are present (*vide* fig. 1, Plate I), which are undergoing active functional change; they contain lipoid, and lie upon a lymphatic space which surrounds the tubule. Reasons are given why it may be assumed that this lipoid substance passes through the basement membrane to the Sertoli cells which contain fine lipoid granules and serve as nurse cells to the spermatozoa.

(5) Microscopic appearances indicate the continuous development of new interstitial cells which mature, actively function and decay. They are present in extreme old age (*vide* fig. 1, Plate IV) and sometimes when spermatogenesis has ceased.

(6) The microscopic examination of the testes of twenty-seven cases of dementia præcox, all commencing in prepubertal, pubertal, or adolescent stages, are described together with the age of admission and duration of asylum treatment, and age at death with cause of death and principal mental diagnostic conditions are given in Table I.

(7) It may be noted that a number of cases died of pulmonary tuberculosis, but a number died of acute disease, e.g., pneumonia and dysentery and after a few days or a week or two of illness. The microscopic conditions did not differ essentially from those dying of pulmonary tuberculosis. In some there was no history of masturbation, whereas in others there was definite information, but the microscopic examination did not reveal any difference.

(8) The regressive atrophy found microscopically corresponded, generally speaking but not always, with the loss of weight of the testes and the naked eye appearances. As a rule the longer the duration of the mental symptoms the more pronounced was the atrophy, but duration of asylum treatment does not strictly connote the length of duration of symptoms.

(9) The regressive atrophy, as determined by microscopic examination, has led me (F. W. M.) to divide the cases into three groups. *The first stage*, in which the changes indicate the formation of normal and degenerate spermatozoa (*vide* fig. 4 and figs. 2 and 3, Plate II) and commencing failure in the formation of normal interstitial cells and by special staining an increase of interstitial fibroblasts. In *the second stage* there is, in addition, an obvious shrinkage of many of the tubules, increase of fibroblasts, thickening of basement membrane and failure of spermatogenesis. The mature interstitial cells are fewer in number and there are numbers of immature cells with pale nuclei deficient in chromatin (*vide* fig. 3, Plate I, figs. F and G, Plate III, and fig. 4, Plate IV). In *the third stage* the tubules either show no spermatogenesis, or only a few tubules relatively show some spermatozoa, some being degenerate; there is a failure of formative nuclear activity and many or (in advanced cases) all the tubules consist only of a very thickened basement membrane lined by Sertoli cells. These cells usually contain lipoid granules in the syncytium, and when this occurs there is lipoid in the interstitial tissue and cells. This indicates that the essential feature of the atrophy is a primary germinal defect.

(10) In seven of the cases of dementia præcox a pigmentary deposit was found in the interstitial cells (*vide* fig. 4, Plate I) which is not seen in normal conditions except in old age, and therefore may be regarded as evidence of pre-senile change.

(11) Table III gives a summary of results obtained in nine cases of psychoses other than dementia præcox, death occurring in post-adolescence. It will be observed that similar appearances of regressive atrophy of the testes occur in many of these as are found in dementia præcox. Three cases of manic-depressive insanity without symptoms of dementia showed normal active spermatogenesis, but apparently a diminution of normal interstitial cells, although death occurred in two of them from pulmonary tuberculosis. In a case of alcoholic dementia, aged 65, the interstitial cells were fairly normal although there was absence of spermatogenesis; the cause of death may account for this.

(12) There are four cases in Table IV in which symptoms of dementia præcox came on in post-adolescence and all of these showed marked regressive atrophic changes of the tubules and the interstitial cells similar to those observed in cases commencing in early life (*vide* fig. 4, Plate I).

A recurrent manic-depressive insanity may terminate in dementia, e.g., No. 6, Table III, and then regressive atrophic changes are found exactly similar to those met with in dementia præcox. Otherwise manic-depressive insanity does not show these regressive atrophic changes in the testes. It will be interesting to see whether there are changes in the brain corresponding to those I have described in dementia præcox in these cases.

(13) As a contrast to these regressive atrophic changes occurring in the biogenetic psychoses are the changes in the testes of cases of general paralysis—an acquired disease. Whereas in the former the atrophy is primary and affects more or less the whole organ, in the latter it is secondary to inflammatory changes in the epididymis, either gonorrhœal or syphilitic, and causing a complete disappearance of the epithelium of the tubules by obstruction of the

vasa efferentia. The result is local patches of dense fibrous tissue affecting especially one testis, sometimes both. In the immediate neighbourhood are tubules showing normal active spermatogenesis and Leydig's cells. Not infrequently amidst the atrophied tubules consisting only of thickened basement membrane are seen nodules and groups of fairly normal interstitial cells.

In spite of this secondary atrophy which affects the testes of so many paralytics, the average weight of the pair after removal of the tunica vaginalis and epididymis is 8 grm. heavier than the testes of cases of dementia præcox. Whereas in the great majority of cases of dementia præcox an emulsion of the testes showed no spermatozoa, the converse was found in general paralysis.

(14) Previous studies show that the changes in the reproductive organs is a part of a generalized germinal defect of durability and vital energy of the whole body most manifest in the brain, especially the cortex, and the reproductive organs.

TABLE II.—PERSONAL CASES OF MR. KENNETH WALKER, F.R.C.S.

Name	Age	Spermatogenesis	Leydig cells
(1) G. C.	59	Active spermatogenesis	Scanty
(2) A. (malignant prostate)	70	Some mitosis and a few spermatids seen	Increase of Leydig cells
(3) T.	57	Spermatogenesis	Scanty
(4) C.	46	Spermatogenesis	Fair number
(5) K.	70	Spermatogenesis	Fair number
(6) H.	80	Absent	Very scanty (this patient had marked mental symptoms)
(7) T.	60	Present	Scanty
(8) C.	60	Present	Fair number
(9) B. (malignant) ...	66	Absent (some mitosis, no spermatozoa)	Scanty
(10) T. (malignant) ...	63	Active	Fair number
(11) K. (malignant) ...	86	Absent	A few degenerating cells only
(12) T.	73	Present (becoming malignant) ...	Scanty
(13) T.	68	Spermatids seen, but no spermatozoa	Very scanty
(14) Cancer Hospital (case of pancreas)	?	Spermatogenesis present ...	Leydig scanty

TABLE I.—DEMENTIA PRÆCOX, TWENTY-SEVEN CASES.

Number of card and name	Age at death	Duration of time in asylum	Diagnosis	Cause of death	Weight of testes in grammes	Microscopic examination
(1) S.A.L.	25	6 months	Dementia præcox; condition remained with slight change; symptoms of a stuporose, hebephrenic form of dementia præcox; has hallucinations and delusions	Acute pulmonary tuberculosis	10-10	Second stage; no normal Leydig cells with low power, pale syncytium in which are numbers of pale chromatin deficient nuclei of varied size and form, a few small cells with eosin staining; interstitial lipid much diminished
(2) W.R.M.	19	6 months	Adolescent insanity; made a violent attack upon his mother; irrational, deluded, sullen and depressed; masturbator	Wasting and exhaustion	8-8	Advanced third stage; no normal Leydig cells with low power, pale syncytium with pale chromatin deficient nuclei of varied form and size, fibroblastic overgrowth; interstitial lipid much diminished
(3) A.	21	9 months	Dementia præcox; threatened to kill his sister, suffered from insomnia, delusions, blind, the result of trying to gouge out his eyes; religious mania	Pulmonary tubercle, aortic hypoplasia	10-11	Advanced third stage; no normal Leydig cells with low power, pale syncytium with pale chromatin deficient or diffuse purple nuclei; excess of fibroblasts; early history of symptoms; but inasmuch as the secondary sexual characters were well developed it follows that the Leydig cells have degenerated since puberty
(4) M.G.	27	18 months (probably duration of symptoms much longer)	Dementia præcox; history of manic-depressive insanity in father; hallucinations, delusions, katatonic; attempted suicide; admits excessive masturbation	Lobar pneumonia	—	Second stage; not much increase of interstitial tissue, groups of eosin-stained cells seen with low power, but fewer than normal
(5) H.W.	21	18 months (for 3 years previously history in the Army of delinquencies)	Recent melancholia; had hallucinations; morose and confused, refuses to speak, with bursts of aggressiveness	Lobar pneumonia	13-8-15-8	Second stage; no Leydig cells seen with low power; isolated small eosin stained cells, pale vacuolated syncytium with oval, irregular pale nuclei deficient in chromatin (<i>vide</i> fig. 3, Plate I)
(6) F.A.E.	28	18 months	Primary dementia, fixed, stupid expression, never speaks unless addressed and then makes silly replies	Dysentery	19-19	Early first stage of regressive spermatogenic atrophy; active spermatogenesis in many tubules, but degeneration of many of the spermatozoa (<i>vide</i> photomicrographs 1 and 2); diminution of Leydig cells as compared with normal, fewer mature cells (<i>vide</i> fig. 2, Plate I)

TABLE I.—*DEMENTIA PRÆCOX, TWENTY-SEVEN CASES (continued).*

Number of card and name	Age at death	Duration of time in asylum	Diagnosis	Cause of death	Weight of testes in grammes	Microscopic examination
(7) L. Wm.	26	20 months	Dementia præcox; dull and apathetic with occasional outbursts of excitement, masturbation	Dysentery and commencing pneumonia (died after a few days' illness)	11-10	Second stage; no normal Leydig cells seen with low power; irregular and oval pale nuclei in vacuolated syncytium pale pink or pigmented; excess of fibroblasts
(8) T.	27	22 months	Dementia præcox; "makes grimaces and laughs without cause . . . wanders about gesticulating and doing strange things," has delusions; dull, stupid, no initiative; no note of masturbation	Broncho-pneumonia	19-16	First stage; no normal Leydig cells seen with low power; numbers of oval, pale, round or irregular nuclei in a pale unstained syncytium
(9) C. U.	24	2 years (about 2 yrs. duration of definite symptoms)	Dementia præcox; auditory hallucinations; violent at times, otherwise stuporose; no mention of masturbation	Broncho-pneumonia	15-16	Third stage; no Leydig cells low power, pale or pigmented syncytium with oval, round imperfectly stained nuclei, fibroblastic overgrowth
(10) H. P.	20	2 years (6 months before admission character changed)	Dementia præcox; duration one year. "attributes present state to a row he had with his brother"; was suspicious	Pulmonary tuberculosis	9-9	Third stage; no Leydig cells, high power, occasionally a pinkish vacuolated syncytium of cells with pale oval and irregular-shaped nuclei, fibrous tissue overgrowth
(11) S. E.	25	2 years	Dementia præcox; "confused, restless. reacts slowly to questions, deluded, dull, apathetic"	Acute lobar pneumonia (death after a few days' illness)	21-2-18-1	Early second stage; only a few small imperfectly stained groups of Leydig cells seen deficiently stained with eosin; there are numbers of oval, round and irregular-shaped pale nuclei, many fibroblasts; fair amount of interstitial lipid
(12) A. M.	25	2 years	Dementia præcox; dull and confused, indifferent to self and surroundings	Pulmonary tuberculosis	10-10	Advanced second stage; generally diminished interstitial lipid; dense interstitial tissue fibroblast overgrowth; ill defined pale syncytium with pale nuclei oval or varied in shape and size, deficient chromatin or diffuse pale purple
(13) G. R. D.	22	2½ years	Dementia præcox; dull, stupid, very rarely speaks to anyone, untidy, habits faulty	Acute pulmonary tuberculosis	15-16	Third stage; greatly diminished interstitial lipid; no normal Leydig cells, vacuolated eosin-stained cells with pale nuclei or vacuolated unstained syncytium with pale, oval, irregular nuclei, deficient in chromatin
(14) S. T.	27	3 years	Dementia præcox; sullen and very taciturn, laughs silly manner, no cause, very impulsive and at times very violent and destructive	Dysentery	12-5-16	Second stage; atrophy of Leydig cells, many cells pigmented

(15) C.	29	4 years	Dementia praecox; "he takes notice of his surroundings"; mannerisms, mutism and periods of impulsive excitement at one time associated with cataleptoid state or katatonia; family history nil	Phthisis	10-10	Third stage; no normal Leydig cells, occasional small isolated cells seen with low power otherwise vacuolated syncytium with pale oval and irregular nuclei; pigment in vacuolated cells
(16) M.J.	29	5 years (commenced before 25 for certain; how long before this not known)	Primary dementia of adolescence; hallucinations, delusions, attitudes missing, grimacing and other signs noted	Acute pulmonary tuberculosis	8-5-9	Third stage; no normal Leydig cells; numerous pigmented cells, pale syncytium with numerous pale nuclei of irregular shape
(17) C.F.G.	30	5 years	Paranoid form of dementia praecox with masturbation, mannerisms, stereotypism; periods of katatonia and excitement	Exhaustion (blue hands and feet at death)	13-5-12	Third stage of regressive atrophy of tubules, no fibroblastic overgrowth; no normal Leydig cells; here and there an islet of Leydig cells seen with oil immersion, cytoplasm pale pink or pigmented; nuclei deficient chromatin, oval or irregular in size and shape
(18) B.	26	5 years	Primary dementia of adolescence; no history of masturbation in the notes	Tuberculous broncho-pneumonia, ulceration of intestines	13-5-11-5	Second stage; very little interstitial tissue and lipid; no normal Leydig cells, pale syncytium with nuclei of varied size and deficient chromatin, a few isolated Leydig cells
(19) S.H.	28	7 years (11 months prior to admission gradually became dull, apathetic and anergic)	Dementia praecox; did not brighten up at all; sat or stood for hours in one position, movements grotesque, showed some stereotypy; much addicted to masturbation before and after admission	Pulmonary tuberculosis	—	Third stage; interstitial tissue increased, islands and islets of Leydig cells containing lipid; Sertoli cells contain abundance of lipid; no normal Leydig cells but vacuolated syncytium containing nuclei of varied form and size, deficient in chromatin, excess of fibroblasts
(20) U.T.	33	7 years	Dementia praecox; dull, listless—only speaks in whispers, occasionally faulty in habits, some katatonia; sits in one place gazing as long as allowed; no masturbation during residence	Chronic dysentery, broncho-pneumonia	8-5-6-5	Third stage; interstitial tissue increased; no normal Leydig cells, vacuolated pale syncytium with here and there groups of pigmented cells; nuclei deficient in chromatin, variable in size and shape; excess of fibroblasts
(21) C.W.J.	35	8 years (about 8 yrs. duration, commenced at 27)	Dementia praecox; history of hallucinations, delusions, masturbation and terminal dementia	Broncho-pneumonia, pulmonary tuberculosis (probably 3 months' duration)	16-15	Early third stage; abundance of interstitial lipid and in Sertoli cells minute lipid granules can be seen passing through basement membrane; lipid granules visible in Leydig cells accounting for vacuolation in haematoxylin-eosin preparation; no normal clumps of cells; with oil immersion pale vacuolated syncytium with pale nuclei of varied form and size; here and there pigmentation

TABLE I.—DEMENTIA PRÆCOX, TWENTY-SEVEN CASES (continued).

Number of card and name	Age at death	Duration of time in asylum	Diagnosis	Cause of death	Weight of testes in grammes	Microscopic examination
(22) M. Wm.	35	10 years	Dementia præcox; two years after admission notes state that he is suffering with secondary dementia; stands in various attitudes in corners of grounds and wards with bowed head; cannot converse rationally, poor idea of time and place	Dysentery	17.5-14.5	Third stage; all the tubules are deficient in epithelial cells, many are only lined by Sertoli cells; a striking feature is the unequal nuclear staining of the remaining cells in the tubules; the interstitial tissue consists of an overgrowth of fibroblasts and a number of pale nuclei of varied size and shape, around which in places are little collections of pigment indicative of degenerated Leydig cells; no normal cells were observed
(23) M.A.G.	27	10 years	At age of 17 certified as mania; year before as suffering with delusions of persecution, possessed by devil, hopelessly lost; attempted to commit suicide; progress of case shows typical dementia præcox	Broncho-pneumonia	20.5-17	Advanced second stage; the most obvious change is an increase of interstitial tissue, excess of fibroblasts; no normal Leydig cells; with oil immersion isolated pale syncytium cells with nuclei deficient in chromatin of varied size and shape, no pigmentation observed
(24) G.A.	36	11 years	Typical dementia præcox of ten years' duration, commenced at 26	Apical tubercle and cholelithiasis	12.0 Left testis absent; left supra-renal 6.5 gram., right 12 gram.	Third stage; increase of interstitial tissue, a few scattered islets of Leydig cells and vacuolated syncytium with pale nuclei of varied form and size, excess of fibroblasts; the spermatogenic cells more profoundly affected than the interstitial cells
(25) W.H.	35	14 years	Dementia præcox; "earned his own living until six years ago," four times sentenced to prison; masturbator; had delusions, hallucinations; was irrational, exalted, incoherent, and had innumerable mannerisms; verbiage; no signs of congenital syphilis	Exhaustion	5.5	Third stage; capsule of testes greatly thickened; seminiferous tubes, extreme regressive atrophy; no lipid in Sertoli cells; nodules of Leydig cells, many containing lipid granules; these nodules stained with hæmatoxylin eosin show a vacuolated syncytium of cells with abundant nuclei of varied form and size containing a fair amount of chromatin, but there is no eosin staining of cytoplasm; the specimen is not unlike that of a cryptorchid (<i>vide</i> photomicrograph, fig. 5)
(26) D.F. Wm.	33	15 years	Dementia præcox; dull, morose and taciturn; tried to cut his throat; sometimes violent and excited; confirmed masturbator	Adherent lungs, probably tubercular	7.5-9	Early third stage; very little interstitial or intertubular lipid; no normal Leydig cells seen
(27) B.F.	35	15 years (15 years' duration at least)	Katatonie dementia præcox; masturbation and adolescence are given as causes; he suffered with emotional indifference, mutism, katatonia and acrocyanosis; did not obey calls of nature, and required constant supervision; destructive tendencies	Acute broncho-pneumonia	10-10	Advanced second stage of spermatogenic atrophy; no normal Leydig cells seen; syncytium with very marked pigmentation everywhere; nuclei varied in size and shape with deficient chromatin excess of fibroblasts; suprarenals very small, deficiency of medullary substance

TABLE III.—SUMMARY OF RESULTS OBTAINED IN NINE CASES OF PSYCHOSES OTHER THAN DEMENTIA PRECOX OCCURRING IN POST ADOLESCENCE.

Number of card and name	Age at death	Duration of time in asylum	Diagnosis and symptoms	Cause of death	Weight of testes in grammes	Microscopic examination
(1) G. J. A.	50	3 years	Subacute melancholia, epilepsy	Broncho-pneumonia; gangrene of lung; epilepsy (Edema of glottis; fatty heart)	9-9	Advanced second stage of regressive atrophy of tubules and Leydig's cells; pigmentation
(2) B. G.	—	18 months	Persecutory insanity	Lobar pneumonia; Exhaustion; bronchitis; emphysema	9-7	Second stage of regressive atrophy of tubes, islets and islands of Leydig cells seen with low power eosin stained, some pigmented
(3) D. E.	48	20 months	? Confusional insanity; serous meningitis; operation for tumour	Exhaustion; bronchitis; emphysema	18-13	First stage advanced of regressive atrophy, atrophous pigmentary degeneration of Leydig's cells
(4) M. T. G.	58	1 month	Melancholia, hypochondriasis	Cirrhosis of liver; carcinomatous; ascites	12-12	Tubules active, spermatogenesis in most of the tubules; nothing abnormal except diminution in numbers of Leydig cells
(5) A. T.	65	22 years	Korsakoff psychosis	Paracentesis	14-14	Complete arrest of spermatogenesis, thickened basement membrane; Leydig cells considering age fairly normal in numbers and staining reaction; not pigmented
(6) N. P.	53	9 years	Recurrent manic-depressive insanity, dementia	Pulmonary tubercle	9-11	Third stage of regressive atrophy of tubules and Leydig cells; pigment granules in syncytium
(7) H.	36	First attack at puberty; four times in Claybury; subsequently 40 days the last time, then died	Recurrent manic-depressive insanity	Acute broncho-pneumonia	?	Many normal tubules showing active normal spermatogenesis and spermatozoa; Leydig cells for the most part pale syncytium with faint eosin staining; some normal groups of eosin-stained polygonal cells seen, some pigmentation, no overgrowth of fibroblasts
(8) H. T. L.	41	History points to alternate periods of depression and excitement. Clinical notes: melancholia, restless, miserable and depressed, a furtive expression; answers questions readily, but becomes incoherent; has hallucinations of sight and hearing; memory fair for remote events, poor for recent events; poor health and condition	History points to alternate periods of depression and excitement. Clinical notes: melancholia, restless, miserable and depressed, a furtive expression; answers questions readily, but becomes incoherent; has hallucinations of sight and hearing; memory fair for remote events, poor for recent events; poor health and condition	Pulmonary tubercle	15-20	Spermatozoa from vesicula alive eight hours after death; many tubules show all stages of spermatogenesis; normal staining and shape of spermatozoa; no failure of nuclear staining; Leydig cells in small clumps seen with low power; oil immersion examination: no pigmentary degeneration; no excess of fibroblasts; occasional groups of normal nucleated polygonal cells well stained; majority vacuolated syncytium with fairly normal nuclei; fair amount of interstitial lipid and in Sertoli cells
(9) B. C.	50	History of attack 4 yrs. previously; present attack 40 days	Manic-depressive insanity	Pulmonary tubercle	10-2-12-2	Vesicula seminalis abundant spermatozoa; spermatic tubules fairly normal for the age; quite one-half show all stages of spermatogenesis; basement membrane not thickened; interstitial tissue much diminished; no excess of fibroblasts; low power only slight evidence of interstitial cells; with oil immersion: a vacuolated faintly pink stained syncytium; nuclei pale, irregular, small creuated as if they had undergone atrophy or were immature; pigmentation of the cytoplasm. Conclusion: interstitial cells affected out of proportion to the spermatogenic

TABLE IV.—PRIMARY DEMENTIA IN POST ADOLESCENCE.

Number of card and name	Age at death	Duration of time in asylum	Diagnosis and symptoms	Cause of death	Weight of testes in grammes	Microscopic examination
(10) V.W.	46	1 week in asylum; history of symptoms 3 years prior to admission to asylum	General paralysis, as he had delusions of grandeur, but blood and cerebro-spinal fluid gave negative reaction, and examination of brain showed no signs of this disease; he made grimaces and had a constant habit of wiping his mouth, and impulsive outbursts like a dementia præcox case; he had no loss of orientation in time and space	Sub-acute dysentery; granular contracted kidneys	11.5-10.5	Vesicula seminalis abundant degenerated spermatozoa; testes: less than normal amount of interstitial tissue; basement membrane of tubules thickened, little evidence of heterotypic mitosis; absence of spermatozoa; the interstitial cells are shrunken, deficient in eosinophil substance; oil immersion examination: pale vacuolated syncytium containing pigment granules; nuclei are pale and deficient in chromatin; a few small eosin-stained cells seen (vide fig. 4, Plate I); the abundance of spermatozoa in vesiculae can be explained by the fact that this is not unusual in dementia præcox; the testes might well pass for a case of dementia præcox in early third stage
(11) B. Wm. G.	52	13 years	Primary dementia; demented, confused, irrational, suicidal, incoherent, hallucinations, grimacing and other symptoms like dementia præcox	Broncho-pneumonia	12.12	Vesiculae small contracted thickened walls, very few degenerated spermatozoa; tubes thickened, basement membrane many only lined by Sertoli cells, no spermatozoa seen; interstitial cells not visible with a low power. With oil immersion: isolated small groups of cells pigmented or vacuolated, nuclei small, pale, irregular and crenated; fibroblasts increased; complete primary regressive atrophy of testis
(12) G. Wm.	56	3 years	Katatonie ecstasy of primary dementia	Chronic renal disease, bronchitis and emphysema; internal hydrocephalus	10.3-10.7	Vesiculae, spermatozoa but degenerated. Many of the tubules show heterotypic mitosis and spermatids, some spermatozoa, but these tubules show a degeneration of the spermatocytes and spermatozoa as if their productive energy had come to an end; there is a disintegration of the cytoplasm and the nucleus; the basement membrane is thickened, and in many tubules there are only spermatogonia and Sertoli cells; the interstitial tissue consists of fibroblasts, and no normal Leydig cells are seen; with oil immersion there are occasional islets of small irregular nuclei; the thyroid weighed only 6.6 grm., probably the increased weight of the pituitary 0.61 may be correlated with this; the suprarenals were only 3.81 and 3.51 grm.
(13) N. E.	44	25 years	Insanity began at the age of 19; he was certified and recertified as suffering with mania, and not until three years prior to his death does dementia occur in notes; throughout the twenty-five years he was in asylum there are periodic notes referring to masturbation, and not until 1913 is he certified as suffering with dementia; the notes state that he speaks in a falsetto voice; attempts were made to cure him of masturbation by blistering the penis	Chronic nephritis and congestion of the lungs	18.5-25 (weight increased by dropsy)	September 20, 1921: oil immersion examination of sections; a few of the tubules show some or all the stages in the formation of spermatozoa, but the great majority exhibit a regressive atrophied condition in all degrees to the final where the whole of the epithelial spermatogenic cells have disappeared leaving only the Sertoli cells. As a general rule the spermatozoa which are found in a good number of the tubules show normal karyokinetic figures. In the loose connective tissue isolated Leydig cells of fairly normal appearance are seen, seldom are groups of normal cells observed, and then never more than two or three; more numerous are cells which have appearance of degeneration or immaturity. There are obvious signs of oedema of the tissue, the lymph spaces in the interstitial tissue and the basement membrane can be clearly seen; doubtless this was caused by the kidney disease, and the oedema of the organs accounted for the weights; the appearances indicate that the weight was more than doubled by the oedema. This specimen shows that there are delicate lymph clefts in the basement membrane. Unlike most advanced cases of dementia præcox the histological changes rather suggest excessive masturbation as the cause, coupled with the effects of the chronic nephritis and oedema.

A British Medical Association Lecture
ON
THE REPRODUCTIVE ORGANS IN RELATION TO
MENTAL DISORDERS.

Delivered to the East Yorks Division of the British Medical Association on February 10th, 1922.

BY
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MR. PRESIDENT AND GENTLEMEN,—Allow me first to thank the East Yorks Division of the British Medical Association for the honour they have done me in asking me to give this address upon the reproductive organs in relation to mental disorders, a subject to which I have recently given much attention. Before proceeding to discuss the facts bearing upon this subject let me call attention to the inborn characters of mind in relation to personality.

The Inborn Characters of Mind.

The furniture of the mind is the memory store of our experiences and the bonds that unite them. The quantity and quality of the furniture of the mind depend firstly upon the inborn germinal raw material begotten with the body and derived from species, sex, race, and ancestry, giving each individual a special predetermined plasticity to receive and store impressions and react to them. This raw material of inheritance upon which psycho-physical energy, durability, educability, imagination, temper, emotivity, moral and aesthetic sense—personality, in fact—so largely depend, is inborn. These fundamentals of mind are begotten with the body and predetermine character and conduct, as was clearly proved by Francis Galton's inquiry into the history of similar and dissimilar twins, which proved that dissimilar twins remained dissimilar in mental and bodily characters when brought up in the same environment, while similar twins brought up in different environment remained similar in mental and bodily characters. This is a convincing proof of the fact that the organic basis upon which the quality of the mind depends is begotten with the body. If inborn good qualities are deficient or absent there will be, in spite of favourable environment after birth, intellectual, aesthetic, or moral feeble-mindedness of various forms and gradations. Again, if there be inherited a disproportion and a lack of harmony and integration of the inborn factors of the raw material upon which mentality is based, an unbalanced mind is likely to develop which will show itself in

various departures in conduct from that of the normal stable individual: it may be in the form of eccentricity, mysticism, fanaticism; or the psychoneuroses—for example, hysteria, neurasthenia, psychasthenia, epilepsy, megrim; or the psychoses (the true insanities)—amentia, confusional or toxic psychoses, dementia praecox, manic depressive or periodic insanity, dementia praesens, and involutional melancholia, as distinct from acquired organic brain disease, such as general paralysis of the insane.

That this tendency to departure from the normal well-balanced mind is largely a matter of inheritance is shown by the study of family pedigrees for several generations, where many or all of these variations from the normal may generally be found in different members of the ancestral stocks. This neuropathic inheritance is often mingled with a streak of genius, especially of the artistic or aesthetic nature.

Photographs of patients showing different forms of insanity were exhibited, including two pairs of sisters with a marked family history of insanity, who were admitted to asylums in early adolescence suffering with dementia praecox, and who are still living and are over 40 years of age. Prior to the war there were 10,000 of the 20,000 odd inmates of the asylums who had been resident for over ten years and 5,000 over twenty years. A considerable proportion of the chronic cases are these cases of dementia praecox.

Neuropathic and Psychopathic Predisposition in Relation to Psycho-physiological Stress.

The study of relatives in the London County asylums by a card system, and by the method of systematic inquiry and construction of a large number of pedigrees, and the investigation of statistical data relating to the age of onset of insanity in the offspring of insane parents, afford to my mind conclusive evidence of three facts in relation to the causation of mental disease:

1. The importance of a neuropathic and psychopathic heredity.
2. The special liability of the neuroses and psychoses to occur in adolescence and the

involution periods of both the male and female sexes, when the sexual function matures and wanes.

3. The influence of child-bearing and lactation in women, acting as exciting causes.

That the inborn predisposition is the most important fact in the development of neuroses and psychoses is also shown by the frequency with which these various psychoneuroses and psychoses occur at periods when normal physiological changes occur in the body—for example, adolescence, when the sex instinct is aroused and matured, and the involution period, when it wanes. Again, in women, pregnancy, parturition, and lactation are normal physiological processes of the sex instinct, yet a number of cases of insanity in women designated puerperal mania or lactation mania occur as a result of a normal physiological process. Even in cases of septic origin predisposition cannot be excluded. For many women have puerperal septicaemia but do not become insane. The term "puerperal mania" is a misnomer in a way, for the cases belong to three groups: (1) Exhaustion psychosis or toxic psychosis, (2) manic depressive insanity, and (3) dementia praecox.

1. The greater the influence of the extrinsic cause, especially if it be pathological—for example, toxic conditions—the more probable is the recovery by treatment removing the source of the sepsis, and less the liability to a recurrence.

2. Emotional shock, worry, anxiety, insomnia, and exhaustion are also regarded as important exciting factors. But the war has shown that these are not of such primary importance as was suspected, for it was observed that there was no great increase of insanity among the women in Galicia and East Prussia when they had to flee on account of the invasion by the Russians in the great war. Moreover, Bonhöffer found only five insane among 10,000 Serbian prisoners who had been subjected to every form of stress of war and disease.



FIG. 1.

If "E" (Fig. 1) represents mental and bodily extrinsic factors, and "I" inborn predisposition, the more of "E" that we can find as a causal factor the more favourable is the prognosis.

Statistical Data Relating to Inheritance and Insanity in the Periods of Adolescence and Involution.

The importance of these physiological states of adolescence and involution in the incidence of the onset of insanity is shown by two graphs (Figs. 2 and 3), based upon an investigation of

the age at the time of first attack in 508 pairs of parents and offspring, from records of 464 insane parents of 500 insane offspring.

These curves in the offspring show 47.8 per cent. of 500 offspring who became insane in adolescence at or before the age of 25. The 47.8 per cent. of cases of adolescent insanity may be divided into four groups:

1. Exhaustion psychosis, confusional insanity, or amnesia, who were discharged recovered.

2. Recurrent insanity—manic depressive—discharged but readmitted on one or more occasions; as a rule the length of the period of asylum detention increases upon each attack, some cases finally passing on to dementia and detention till death.

3. Primary dementia of adolescence or dementia praecox. In the vast majority of cases progressive and permanent detention till death; these cases make up a large proportion of the chronic lunatics in asylums.

4. The imbeciles are relatively few in number, as they are sent to the asylums of the Metropolitan Asylums Board. A few are admitted to the London asylums on account of the onset of acute symptoms. There are also a few cases of juvenile general paralysis, but the great bulk of the cases belong to 1, 2, and 3, and especially 3.

These statistical data were prepared in 1911.

In 1917 I made a further analysis of relative cards since 1911, a period of six years. This analysis was limited to insane parents of offspring, of which a diagnosis of dementia praecox was made, and instead of 47.8 per cent. there were 75 per cent. of the 69 cases diagnosed as dementia praecox admitted at the age of 25 or under (Fig. 4). Seeing that a great many of these cases were either insane before certification, or by their conduct had given prodromal evidence of oncoming dementia, it is highly probable that all the cases really commenced in the adolescent period.

Prior to the war the two sexes were about equally represented in the admissions. During the war the male cases of dementia praecox were diminished by one-half. This may easily be accounted for by the fact that a number were conscripted in the undiagnosed early stages of the disease, or the disease developed after their admission to the army. It was found that 14 per cent. of the total insane who had served in the army were cases of dementia praecox, which proves the truth of the assumption I have made in respect to the great fall in the admissions on the male side during the war.

A comparison of the two curves of the parents shows a notable difference. The curve of the fathers does not commence to rise till after 25, and the 30-40 peak corresponds with the incidence of general paralysis of the insane (Fig. 2). It may here be remarked that males suffering with general paralysis are four to five times as numerous in the asylums as females, but this does not account for the main difference in the curves of fathers and mothers. This is due to

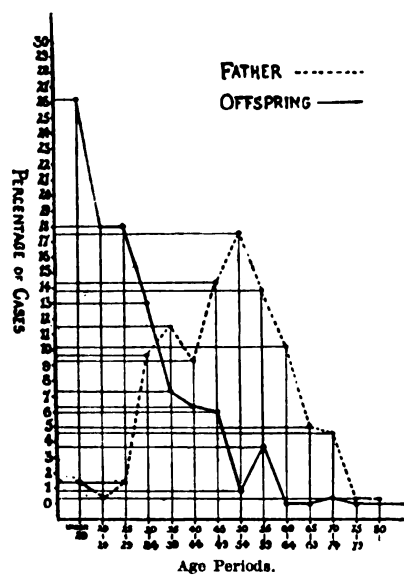


FIG. 2.

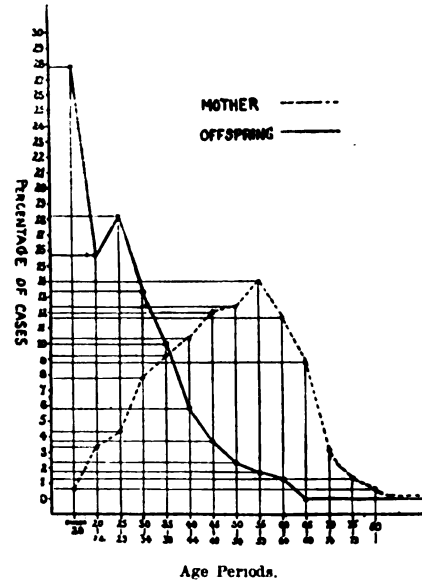


FIG. 3.

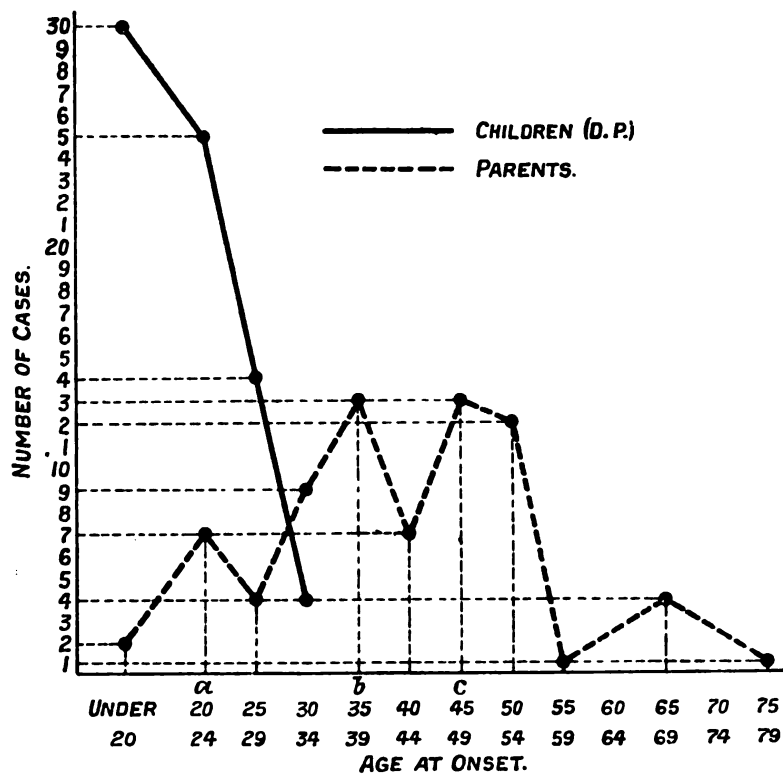


Fig. 4.—Broken line=ages of parents upon first attack of insanity. Uninterrupted line=ages of offspring upon admission to asylums.

the incidence of child-bearing and lactation, which causes a steady continuous rise to the climacterium in the maternal curve (Fig. 3). The 50-60 peak corresponds to the involutive period.

It was also computed that only 7.9 per cent. of the children were born after the first attack of insanity in the parent.

Recurrent Insanity in Women and Child-birth.

An analysis of 642 female admissions to three London County Council asylums during the year 1911 showed 148 recurrent cases, of whom 32 (21 per cent.) had children between their respective dates of admission. The inference that can be drawn is that rather less than one-fifth of the recurrent cases have children after their first attack of insanity. This may be explained by the adoption of contraceptive methods, but my investigations suggest another important cause—namely, early involutional changes in the ovaries in all the psychoses.

Two Schools of Thought in Relation to Dementia Praecox: the Psychogenic and Physiogenic.

There are two schools of thought—one physiogenic, the other psychogenic; the former attributes the mental disorder to a bodily pathological condition, the latter to a non-adaptable psychological function. The frequency with which psychoses and psychoneuroses follow emotional shock connected with the sex impulse, the character of the dreams and their interpretations, the nature of the hallucinations and delusions in a great number of the cases suggest an origin in excitement or repression of the sex instinct.

Because by the aid of the microscope we cannot show an organic cause in epilepsy, neurasthenia, or hysteria, and other psychoneuroses, it does not follow that the deranged mental function is not due to deranged bodily function. It was thought, and is still, by the psycho-analyst school that in the primary dementia of adolescence—dementia praecox, as it is called—there were no bodily changes sufficient to account for the signs and symptoms of mental disease. The physiogenic changes that are met with, it is stated by Jung, are the result, not the cause, of the psychogenic disorder. Thus this author in his work *Analytical Psychology* states:

"The difference between us is as to the question whether, in relation to anatomical basis, the psychological disorders should be regarded as primary or secondary. The resolution of this weighty question depends upon the general problem as to whether the prevailing dogma in psychiatry—'disorders of the mind are disorders of the brain'—presents a final truth or not. This dogma leads to absolute sterility as soon as universal validity is ascribed to it."

And—

"Such an idea is only incomprehensible to those who smuggle materialistic preconceptions into their scientific theories. This question does not even rest upon some fundamental and arbitrary spiritualism, but upon the following simple reflection. Instead of assuming that some hereditary disposition, or a toxæmia, gives rise directly to organic processes of disease, I incline to the view that upon the basis of predisposition, whose nature is at present un-

known to us, there arises a non-adaptable psychological function which can proceed to develop into manifest mental disorder; this may secondarily determine organic degeneration with its own train of symptoms. In favour of this conception is the fact that we have no proof of the primary nature of the organic disorder, but overwhelming proofs exist of a primary psychological fault in function, whose history can be traced back to the patient's childhood."

But when doctors speak of psychogenic, what do they mean? The furniture of the mind is made up of past experiences and the bonds that unite them, but there can be no mind without memory, and there can be no memory without body. All psychical processes are subordinate to physiological processes, and all physiological processes are associated with, and dependent upon, oxidation processes. That the mind reacts on the body and the body on the mind is certain, and that the bodily symptoms of many functional neuroses, such as hysteria and anxiety neurosis, can be cured by suggestion and persuasion is certain. In the former of these conditions we have a perseveration of an idea, brought about by auto-suggestion or hetero-suggestion; in the case of the conscript it was an unconscious defence mechanism connected with the instinct of self-preservation; in civil life it is connected with the sex instinct in the majority of instances. The anxiety neuroses are, in a number of instances, dependent upon a wound of the *amour-propre*.

Time, however, will not permit me to do more than refer to the psychoneuroses, and I shall devote my attention to mental diseases which may be directly associated with the function of reproduction.

The Insanity of Adolescence.

The insanity of adolescence was first described by Clouston, who recognized two types—a curable, and an incurable which went on to progressive dementia. To this latter type was given the name "dementia praecox" by Kraepelin, who divided it into three clinical groups: the katatonic, the hebephrenic, and paranoid. Whether such a classification is justifiable or not on these lines is open to question; it is certainly of less value to know what a thing is called than to know what it is, and to find out how it has come about that an individual's mind is deranged. This can only be effected by careful investigation to ascertain what an individual was born with and what happened after birth, and in this respect psychological inquiry to ascertain the development of the mind is as necessary as to know the development of the body. It may be, as Jung says, that a primary psychological fault in function, whose history can be traced back to childhood, will be found in most of these patients. This fault, he would say, is a predisposition of which we know nothing. I would urge that there is evidence to show that, at any rate in dementia praecox, there is an inborn genetic lack of durability and reproductive formative activity. Kraepelin discusses and discards the idea that this disease is due to masturbation, and does not, as Clouston did, recognize a "masturbational insanity." Onanism, according to Kraepelin, is

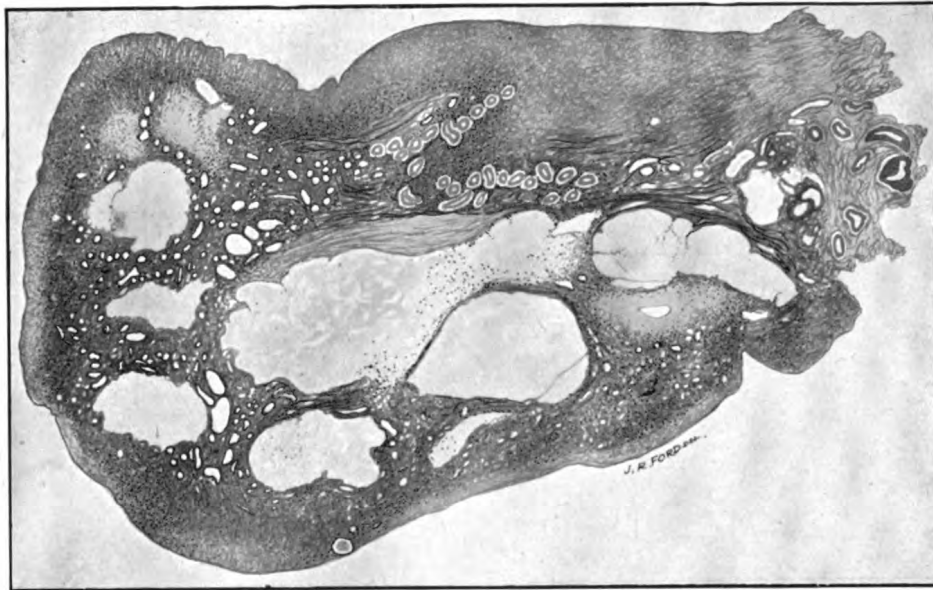


FIG. A.—Ovary of G.; dementia praecox. Age at first attack, 25; pregnant seven months; died eighteen months later. Weight of ovaries, 3 grams and 2 grams. Old corpora lutea vera; thickened vessels indicative of involutional change; no maturing Graafian follicles; one small degenerated immature follicle on the surface; very few primordial follicles left (Fig. C). (Magnification 10×1 .)

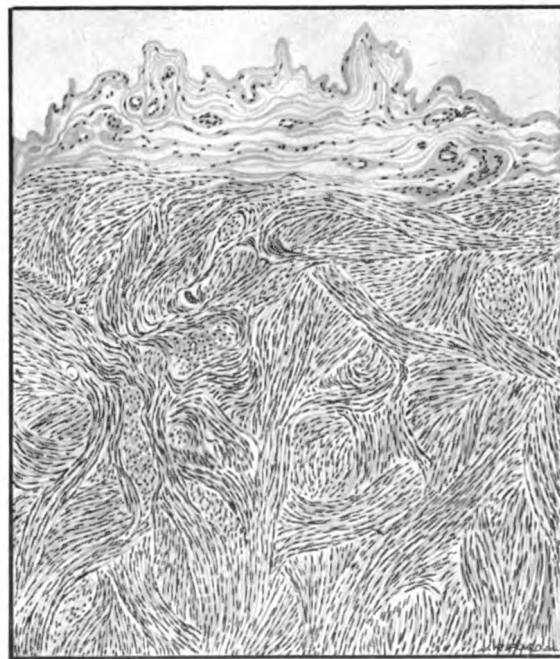


FIG. B.—Portion of cortex of ovary, showing complete absence of follicles — sclerosed fibrous irregular surface with dense stroma beneath. (Magnification 100×1 .)

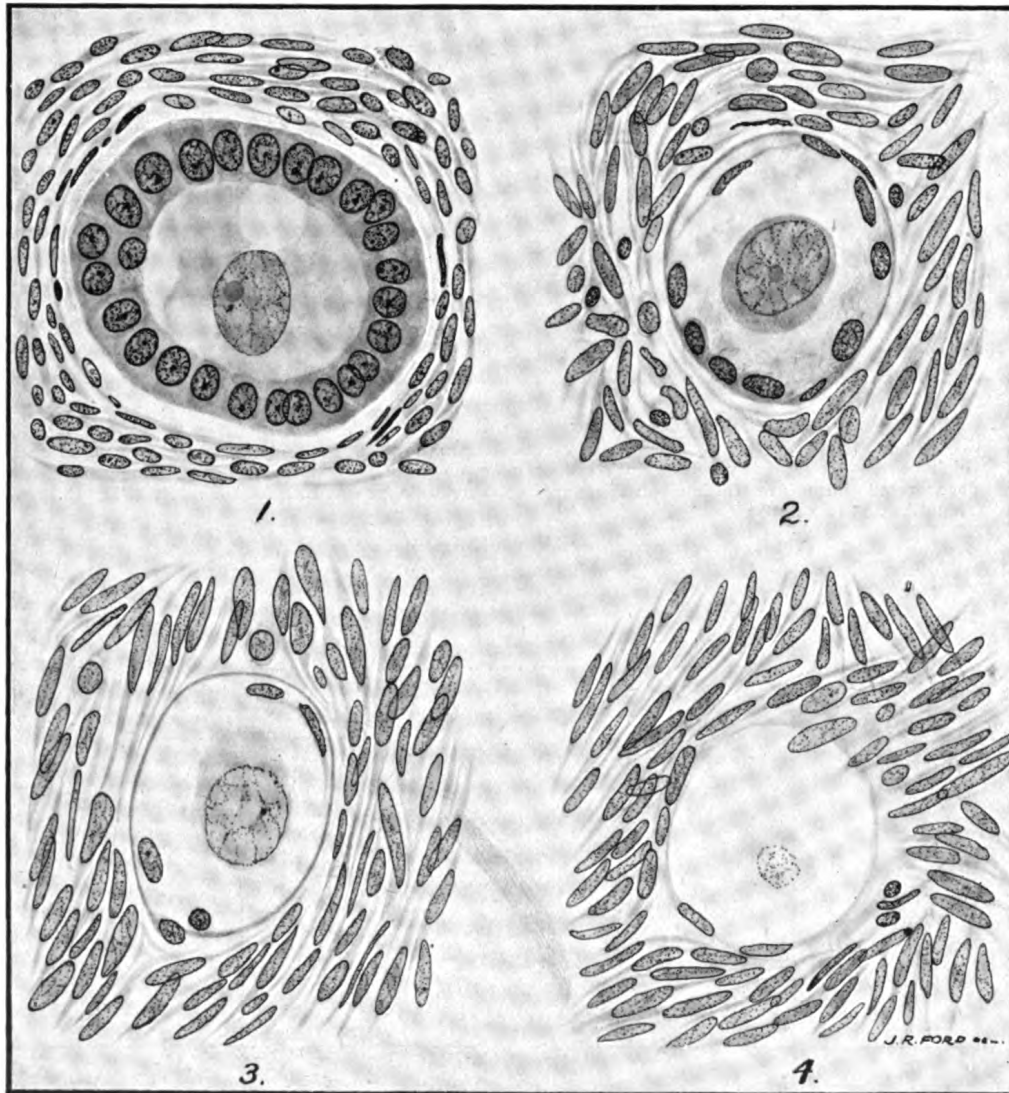


FIG. C.—Four primordial follicles. These were in a group and show: (1) Lining epithelial cells intact containing ovum with oval swollen nucleus; the epithelial cells of the zona granulosa have already separated from the theca interna, a sign that further maturation will not proceed. (2) Lining epithelium degenerated. (3) The same more marked. (4) Commencing ingrowth of stroma. This group was the best that could be found. (Magnification 800×1 .)

a symptom; but it may be a contributory cause of the mental disorder. Most psychiatrists recognize the association of the disease with the sexual functions. Kraepelin, Urstein, and other authorities suggest toxins from the sex glands as a probable cause of the mental disease.

Morbid Histological Changes in the Brain.

Most psychiatrists accept the findings of Nissl, Alzheimer, and those who have followed them in associating the mental symptoms with the microscopic changes in the ganglion cells of the cortex, mainly affecting the nucleus and causing thereby a defective metabolism and function of the ganglion cells with pigmentary or lipoidal degeneration, akin to that met with as a result of senile change.* Jung, as we have seen, takes an entirely different view of this question.

The Physiogenic Explanation of the Vital Impulse in Relation to Mental Disorders.

I have endeavoured by my researches to show that the mental breakdown in adolescence, in the puerperal and lactational states in women, and in the involutive period in both the male and female sexes, is due to a failure of the vital impulse (*élan vital*) or libido of the psycho-analysts. But this vital impulse is an inborn character, and, like longevity and durability, it is due to bodily conditions. Up to puberty, this vital impulse is manifested in the psycho-physical reactions for self-preservation by nutrition for the growth of the body and for its defence against injury. But Nature is unmindful of the individual, mindful only of the species, and the body is, after all, but the vehicle for the germ cells, so that all the vital energy over and above that which is necessary for the functional activities of the somatic tissues is in adolescence available as psycho-physical energy for the formative productive energy required for reproduction. In adolescence a complete mental revolution occurs peculiar to each sex, and the vital impulse is now directed mainly towards the fulfilment of the instinct of propagation, as well as, and even more than, self-preservation. The vital impulse to psycho-physical activities is manifested in new emotions, passions, and sentiments, and the reactions are peculiar to each sex. If these sex activities are not frustrated and repressed, which so often happens, owing to the taboo of society, and the disharmony which exists between physiological sex relations and social customs, usages, and traditions, the sex impulse to propagate is accompanied by a *joie de vivre*, "a new and unaccustomed spirit," an *élan vital*, so admirably expressed by Shakespeare in *Romeo and Juliet*:

"My bosom's lord sits lightly on his throne;
And all this day an unaccustomed spirit
Lifts me above the ground with cheerful thoughts."

Now what will happen if there should be a suspension or suppression of this libido or vital

(love*) impulse due to an inherent potential deficiency or owing to physiological stress or pathological conditions? In what structures of the body should we expect to find evidence of functional organic deficiency? We should expect to find a deficiency of organization in the germ cells, for it is by them that the vital energy is genetically transmitted. This energy, characteristic of every living organism, to build itself up according to a certain inherited type or pattern, is embodied in the nuclear substance of the fertilized ovum derived from the male and female gonads, in virtue of which it can turn to account both the food and the force which it derives from without. The productive energy, which in the normal male is manifested by an almost unlimited nuclear formative spermatogenic activity for more than two-thirds of a man's life, and in the normal female by a fertility and capacity of bearing and nourishing offspring, the mother remaining in good mental and bodily health during the reproductive period, denotes an inborn endowment of formative vital energy.

It follows that evidence of a primary regressive atrophy of the spermatogenic functions, and of a regressive atrophy and failure of the primordial follicles of the ovary to develop Graafian follicles, is indicative of an hereditary deficiency of the genetic vital impulse. Now I have shown in a large number of cases of dementia praecox, in both the male and female sexes, that a primary regressive atrophy of the reproductive organs occurs. In the female the disease is often manifested after the birth of the first child. Thus the woman suffers with puerperal mania which terminates in dementia, from which the patient never recovers, although she may with care live a vegetative existence for a number of years in an asylum. Can anything more tragic happen to a young husband than this? Yet I have investigated not a few such cases of puerperal mania, terminating in dementia praecox, affecting a young married woman after the first confinement. Some few of the cases occurred in unmarried women, sometimes of the imbecile type. Emotional shock and social degradation may in such cases act as exciting factors in the production of the mania. In these cases of post-puerperal dementia I have found in the ovary macroscopic and microscopic evidence of failure of reproductive power. The organs are small, shrivelled, and densely fibrous, showing no Graafian follicles, a totally different appearance from the ovaries of a young woman dying of acquired organic brain disease—for example, general paralysis of the insane. Microscopic examination shows a few old corpora albicantia or corpora lutea, but no recent follicle formation; the primordial follicles are greatly diminished in numbers and are seen in all stages of degeneration and replacement by the fibrous stroma. Examination of the nucleus (germinal vesicle and germinal spot) of the ovum shows a deficiency in the chromatin substance, consequently indicating a failure of the productive vital energy necessary to stimulate the development of the zona granulosa cells and formation of the Graafian

* Lantern slides were shown illustrating these changes, for a full account of which the reader is referred to "Studies in the Pathology of Dementia Praecox."

* Used in the broad sense of Jung.

follicles. This nuclear defect in the female germ cell has been said to be due to the effects of chronic disease—for example, tuberculosis, from which so many of these patients die; but we know that tuberculous women are not infertile and do not develop mental symptoms—indeed, the tuberculous woman while pregnant seems to put forth a supreme effort of the body to resist the disease, and thereby enables the child to develop and be born alive, afterwards to be followed by a “rapid decline” and frequently death of the mother, which to my mind affords a proof that every cell of the body has an organized impress—or, if you like, a pre-organized mneme—that its great mission is the preservation of the species. A more direct argument, however, against chronic disease being the cause of the ovarian regressive atrophy is that occasionally I have had a case of dementia praecox in a female who was in good bodily health, and died of acute disease after a few days’ illness. I have found the same atrophic changes and fibrotic substitution as in the cases dying of chronic disease. In the ovaries of a general paralytic woman, dying before the involutive period of life is reached, although she may have suffered with chronic disease for years before death, yet we shall find evidence, especially if she is a married woman, of numbers of corpora albicantia and of corpora lutea, a history of having had a number of children, in some instances miscarriages or abortions, or children born dead—the result of the syphilis. The evidence of an inborn germinal defect is, in the greater number of cases, absent in general paralysis. There is no primary regressive atrophy of the ovaries. In spite of the mental and bodily disease from which she suffered, the ovaries usually show follicles undergoing development in all stages; most of them, however, become atretic. In the dementia praecox cases there is usually no sign of atretic follicles, although there are old corpora atretica (see Plate, Fig. C, 1, 2, 3, 4).

Dr. Iris Fox has been good enough to abstract the notes of my observations upon a large number of ovaries in various forms of insanity. The conclusions are highly suggestive of the fact that all forms of insanity are associated with a tendency to failure of reproductive power and early involution, yet we know that chronic disease will produce the same effects. Still there can be no doubt that dementia praecox, an inborn disease, shows this loss of reproductive power to a far greater degree than general paralysis of the insane, an acquired disease, which accords entirely with my observations on the testes in these two diseases.

Summary of Results from Examination of Clinical and Pathological Data of 97 Cases of Patients under 50 Dying in Asylums and of 8 Dying in Hospital.

I.

(a) Diminished follicles occur in most types of mental disease and in many controls. The details suggest that this diminution may be a more constant feature of dementia praecox than of the other forms of insanity.

(b) Sclerosis (which has been assumed to be absent when not noted) is also common, but is remarked in a much higher proportion of the dementia praecox cases than in any other disease.

(c) Vascular thickening may accompany sclerosis, or occur independently (for example, in general paralysis of the insane).

II.

Degeneration of follicles is found in a very high proportion of all the ovaries examined. No deduction can therefore be drawn from it here.

III.

The nuclear condition of ovum has been noted in 44 cases. The figures show a high proportion of cases of nuclear degeneration in dementia praecox. The other figures are too small for generalization, but suggest a special freedom from degeneration of the nuclear chromatin in general paralysis. With regard to other mental diseases there is no evidence here to show that they differ in this respect from dementia praecox. The figures suggest that the nuclear degeneration is probably unrelated to circulating differences, since the general paralysis of the insane cases show a fair number with vascular degeneration. The figures, however, are too small to establish this point.

IV.

(a) Some degree of maturation of the follicles is present in the great majority of cases, the exceptions being almost always cases of dementia praecox, or (2) dementia praecox.

(b) No clear deductions seem possible from either the corpus luteum content or the menstrual history—from the former because the type of corpus luteum is not generally noted, and, if it were, its dating would be somewhat empirical; from the latter because of the possible inaccuracy of the record.

(c) Shows a connexion between the duration of the disease and ovarian change as a rule. But this does not establish any special relationship beyond that existing between other chronic and acute diseases and ovarian function.

I am at present pursuing the investigation by an intensive study of the ovaries and endocrine glands in a number of cases in which adequate clinical data have been obtained. So far as the investigation has proceeded, regressive atrophy of the ovarian functions is a marked feature of dementia praecox.

Now if we turn to the male adolescent who develops dementia praecox—and I have investigated now the testes in thirty fatal cases, and in many of these the brain and endocrine glands—we find evidence of a primary regressive atrophy. The first account of these investigations was published in the *BRITISH MEDICAL JOURNAL*, vol. ii, 1919, pp. 655, 698, 737, under the title “Normal and Morbid Conditions of the Testes from Birth to Old Age in 100 Asylum and Hospital Cases,” and subsequently in “Studies in the Pathology of Dementia Praecox,” *Proceedings of the Royal Society of Medicine*, vol. xiii, 1920, Section of Psychiatry; “The Psychopathology of Puberty and Adolescence,” Morison Lectures, 1921; “Second Maudsley Lecture”; published in the *Journal of Mental Science*, July, 1921.

I will briefly summarize the results of these investigations together with the results of a further investigation on dementia praecox and other psychoses, especially in relation to the interstitial cells of Leydig, which is now in the

press and will be published in the next number of the *Proceedings* of the Royal Society of Medicine. There is, generally speaking, a correspondence between the degree of regressive atrophy of the testes and the duration of the mental symptoms. The atrophic process may result in all stages of failure of nuclear formative activity of the spermatogenic epithelium terminating in a complete disappearance, leaving only the Sertoli cells. There are also profound nuclear and cytoplasm changes in the interstitial hormone cells. This primary atrophy resembles the changes met with in the testes of cases of involutional melancholia, post-adolescent dementia praecox, and terminal dementia and manic depressive insanity. Besides the failure of spermatogenesis, there is pigmentary degeneration of the interstitial cells in 25 per cent.

of the cases of dementia praecox dying in adolescence, a sign of senile decay. This regressive atrophy was not found as a rule in general paralysis and other forms of organic brain disease. These investigations appear to show that in the male and female suffering with these various psychoses there is a failure of the vital formative impulse of reproduction, especially marked in cases presenting the clinical signs and symptoms of dementia praecox. Lantern slides were exhibited in illustration of these facts, and the reader is recommended to consult the communications referred to for further precise and detailed information.

In conclusion, it may be noted that these observations on regressive atrophy of the male reproductive organs have been confirmed by the researches of Tiffany.

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An Address
ON
BODY AND MIND:
THE ORIGIN OF DUALISM.

*Delivered before the Medical Society of Charing Cross
Hospital on Tuesday, Dec. 13th, 1921,*

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THE problem of body and mind, or body and soul, is as old as civilisation. The evolution of language has led to a dual terminology, the origin of which I shall point out later. So long as man analyses his own feelings, so long must he use language in order to express to others his thoughts and so long must he have two sides to his nature—a bodily and a mental side; accordingly he is accustomed to accept this duality as obvious. At the present time human beings, with few exceptions, accept this duality of body and mind, and language is accordingly impressed with the idea of dualism, and we should not be understood by the majority of people if a new terminology were invented.

Dualism has been reaffirmed by experimental psychologists of the Wundt school, who have advanced the doctrine of psycho-physical parallelism which teaches that the series of bodily events and the series of psychic events stand in an inseparable correlation to one another; but that body and mind, though existing side by side, are separate. This is really a modification of the pre-established harmony of Leibnitz, which Kant had already expressed in a special form. Now if we inquire into the origin of this dualism which exists in all human beings—savages, primitive people, or cultured people—we shall see that it is centred around death; the evidence of burial rites and customs universal in the bronze and neolithic ages shows that prehistoric man believed in an intangible invisible spirit which left the body at death. The doctrines of the wandering souls of the Egyptians, of the stories of the Old Testament, of Homer, who speaks of life “flitting away like a dream,” affirm that the body and soul are separable, are two different things, which during life stand in close connexion with one another, but which are separated at death. There was also the prevalent belief that evil spirits could take up their abode in the body; insanity was thus accounted for, and it appears

from a recent letter in the press that there are even doctors of the present day who believe in demonology. I suppose general paralysis of the insane in older days would have been attributed to an evil spirit, but we now know that it is due to the spirochæte of syphilis which has taken up its abode and multiplied in the brain.

It is probable that dream life has played a considerable rôle in the foundation of the belief in a soul which can leave the body and return ; for in dreams people are carried away to far distant lands, talk to their friends, see and converse with those long since dead : and a natural inference is that in sleep some spirit leaves the body and wanders away—something invisible which has sensibility, feels, thinks, and acts, the same thing that leaves the body at death. This invisible, intangible something, the soul, is either feared or honoured, and the whole mode of abstract thought of primitive people is centred round this point of view.

The problem of body and mind, and body and soul, was discussed by the ancient philosophers, and it is interesting to observe that the doctrine of Lucretius, based partially on the teaching of Democritus and Leukippos, was monistic. He considered the soul to be the vital impulse of all the organs and tissues of the body. The mind is in the head which directs and controls the whole body. He states that "the mind is begotten with the body, grows up with it, and grows old along with it." There is much truth in this doctrine of Lucretius.

THE INBORN QUALITY OF MIND BEGOTTEN WITH THE BODY.

The furniture of the mind is the memory of experiences and the bonds that united them from infancy onwards. But the inborn characters play a very important part not only in the development of the body, but also in that of the mind. These inborn qualities are psycho-physical energy, educability, imagination, emotivity, temper, and a mental balance which depends upon harmonious interrelation and integration of those qualities of the soil upon which the mind grows up along with the body. The inborn germinal qualities are dependent upon sex, race, and ancestry, and combined impress a personality on every individual which profoundly affects his reaction to environmental influences in response to the three primal instincts of self-preservation, propagation, and the herd instinct of conforming to social customs, traditions, and usages. Galton's inquiry into the history of similar and dissimilar twins showed that mental and bodily resemblances occurred in similar twins, and that whereas dissimilar twins brought up under the same environmental influences remained dissimilar as regards the innate qualities of mentality, similar twins brought up under different environmental influences remained the same. Before considering the mind in relation to the study of the

brain in mental deficiency I will give a short description of the history of the brain as the seat of the psyche or soul.

THE BRAIN AND THE PSYCHE.

Aristotle considered that the psyche was in the heart and that the brain was a cooling organ. Hippocrates, the father of medicine, localised the psyche or mind in the brain, and this doctrine was upheld by Galen. Most authorities of the Middle Ages accepted the doctrine of Galen that the brain is the organ of mind or psyche; the Cartesian doctrine—according to which the mind was regarded as an invisible, intangible something inhabiting the body and not to be dissociated from the brain—localised the soul's dwelling place in the hollow spaces (ventricles) of the brain. Descartes, wishing to materialise the soul and being unable wholly to discard the Cartesian doctrine, localised the soul in a small gland, the pineal, situated in the centre of the ventricles. Swedenborg, profiting by the discovery of the compound microscope by Leuwenhoek, localised the psyche in the cells of the great brain (cerebrum); these cells, of which there are millions, he called cerebellula. Then came Gall, who argued that the mind must be in the great brain seeing that man's faculties were so much superior to those of animals, and that the great difference between the brains of men and the brains of animals was in the size of the cerebral hemispheres. He also demonstrated the fact that this part of the brain was diseased and wasted in lunatics and idiots; the remarkable work of Gall is forgotten, and his name is generally associated only with the exploded doctrine of phrenology. In 1876 came the experiments of Fritsch and Hitzig, and later of Ferrier, and the establishment of the doctrine of cerebral localisation; although the clinical observations of Dax and Broca, of Bastian and Wernicke, had demonstrated the fact that injury or disease of the left hemisphere in right-handed persons led to various forms of aphasia according to the seat of the lesion, and Hughlings Jackson by clinical observations had foretold localisation of movements in the cortex. It was hoped that further observations in this direction would lead to the understanding of the higher functions of mind in relation to body.

THE THEORY OF EVOLUTION AND ITS INFLUENCE ON PSYCHOLOGY.

But it was Darwin's theory of evolution and descent of man which revolutionised biological science and led to the greatest advance in our knowledge of body and mind. His theory dispensed with dogma and tradition, enabling psychology to be placed under the biological sciences, with the result that many of the younger psychologists—especially those who are concerned with the study and treatment of disorders

and diseases of the mind—have regarded psychology from a biological point of view. A pioneer in that direction was Henry Maudsley. In support of this view I will quote a passage from the "Descent of Man" (p. 70):—

"It has I think now been shown that men and the higher animals, especially the primates, have some few instincts in common. All have the same senses, intuitions and sensations; similar passions and even the more complex affections and emotions, such as jealousy, suspicion, emulation, gratitude and magnanimity. They practise deceit and are revengeful. They are sometimes susceptible to ridicule and even have a sense of humour. They feel wonder and curiosity; they possess the same faculties of imitation, of attention, deliberation, choice, memory, imagination and association of ideas and reason, though in very different degrees.

The individuals of the same species graduate in intellect from absolute imbecility to high excellence. They are also liable to insanity, though far less often than in the case of man. Nevertheless, many authors have insisted that man is divided by an inseparable barrier from the lower animals by his mental faculties. I formerly made a collection of about a score of such aphorisms, but they are almost worthless, as their wide difference and number prove the difficulty, if not the impossibility, of the attempt. It has been asserted that man is alone capable of progressive improvement. That he alone makes use of tools, of fire, domesticates other animals, or possesses property; that no animal has the power of abstraction or of forming general concepts, or is self-conscious and comprehends itself; that no animal employs language; that man alone has the sense of beauty, is liable to caprice, has the feeling of gratitude, believes in God, or is endowed with conscience."

Darwin says: "I will hazard a few remarks on the more important and interesting of these points." He then gives a number of examples in animals in support of his theory. At the same time he admits freely that no animal is self-conscious, if by this term it is implied that he reflects on such points as whence he comes or whither he will go, or what is life and death, and so forth. But how can we be sure that an old dog with an excellent memory and some power of imagination, as shown by his dreams, never reflects on his past experiences, pleasures, and pains in the chase? This would be a form of self-consciousness. On the other hand, how little can the hard-worked wife of an Australian savage, who uses very few abstract words and cannot count above four, assert her self-consciousness and reflect on the nature of her own existence?

Remarking upon language, Darwin observes that the dog expresses in five or six different barks or tones our cries of pain, fear, surprise, anger—together with their appropriate actions; and the murmurs of a mother to her beloved child are more expressive than any words. Mr. Leslie Stephen says that a dog does frame a general concept of cats or sheep and knows the corresponding words as well as a philosopher; and the capacity to understand is as good a proof of vocal intelligence, though in an inferior degree, as the capacity to speak. The difference in mind between man and the higher animals, great as it is, is certainly one of degree and not of kind (Darwin).

THE PRIMAL INSTINCTS COMMON TO MEN AND ANIMALS.

There are three primal instincts common to men and animals: self-preservation, propagation, and the herd-instinct; and these three instincts are the springs from which the streams and rivers of mental activity flow. From the biological point of view we must regard the body as a commonwealth of cells which has developed from a single cell—the fertilised ovum. Whether we trace its development ontogenetically or phylogenetically, we see the same order of things—increasing complexity and differentiation of structure and function, which necessitates an increasingly complex harmonious interrelation and integration of function for the commonwealth of the organism. In this respect it is very much like the social organism. This harmonious interrelation is brought about by (1) bio-physical processes in the nervous system, and (2) by bio-chemical processes in the organs and tissues of the body, the products of which are conveyed by the blood and lymph streams. Whereas cerebro-spinal sensorimotor processes can be precise, discriminative, and limited in intensity and duration, and therefore capable of infinite variety and refinement by progressive evolution, the bio-chemical processes—although capable of an extraordinary discriminative sensitivity—must be diffuse in their effects, unless they act indirectly through the nervous system. Although the brain is the organ which stores the memory of past experiences and the bonds that unite and recall them, thereby enabling the individual to adapt himself to environment in the struggle for existence, yet strictly speaking the mind is directly dependent upon the vital activities and harmonious interactions of all the organs and tissues of the body; for of what use would the brain be without the peripheral sense-organs and the nerves which connect them with the brain and spinal cord? These are the avenues of intelligence, as was clearly recognised by Aristotle in his famous dictum: *Nihil in intellectu quod non fuerit prius in sensu*," which would be more correct if *et in motu* were added. But another fundamental function of the brain, besides the life of external relation, is the consciousness of the individual's own personality, his appetites and desires, which are due in great part to the organic and bodily sensibility which without cessation makes him aware of his existence and needs.

THE VITAL IMPULSE.

The vital impulse is in every part of the body, and it is certain that the more active the vital impulse in an organ or structure the greater automatically is the supply of oxygen by the blood. Every particle of the body is as much alive as the whole and possesses a bio-chemical memory. In proof of this we know

that immunity against disease is due to the body having once defended itself against the toxins of a pathogenic micro-organism; its tissues are thereby sensitised against this particular poison, so that should the organism again attempt to enter the body the defensive mechanisms are immediately mobilised and the organism destroyed before it can multiply in the body. Still more remarkable is the condition termed anaphylaxis or an acquired hypersensitivity of the organs and tissue of the body against foreign substances, especially proteins. Thus, if horse serum is introduced into the body all the tissues of the body are sensitised to resist this foreign substance; and this sensitivity, which is connected with colloidal changes in the tissues, increases day by day, so that after a week or ten days, especially in certain people with an idiosyncrasy, the introduction of a fresh dose of horse serum produces such an intense colloidal reaction in the tissues that shock, sometimes fatal, may occur.

EVOLUTION OF A SPECIFIC BIO-RHYTHM IN THE NERVOUS SYSTEM.

A physical or chemical stimulus, connected with the primal instincts of self-preservation by the avoidance of pain and the capture of food, of propagation and of the bonds of union of the herd, has continued for countless ages in the process of evolution and survival of the fittest, and a specific bio-rhythm to particular stimuli subserving these primal instincts has become fixed and organised in the bodily structures, especially of the nervous system, constituting thus a physiological basis for instinctive action. Associated with these primal instincts are the primitive emotions, or certain states of feeling and bodily reactions common to men and animals. These instinctive reactions may take place independently of consciousness—e.g., the decerebrate dog will, if it be injured, attempt to run away and it will turn its head round and show anger by exposing its canine teeth. Again, Goltz showed that a dog which had had the whole of its brain cortex removed had completely lost its memory, for it invariably showed anger at the approach of the man who daily fed it. This same dog also exhibited the emotion of disgust, for nothing would induce it to eat meat made bitter with quinine—not even starvation.

The higher we rise in the evolutionary scale the more are these instinctive reactions brought under control by the highest functions of the brain. But Nature is unmindful of the individual and mindful only of the species, and in order that the self-regarding sentiment of man should not outweigh the instinct of propagation has predetermined an urgent desire and attraction to the opposite sex accompanied by intense pleasure in the gratification of the sexual appetite. This desire, upon which so many of our mental activities directly and indirectly depend, is primarily due to the sensitising influence of bodily structures on the brain, and

I will now dwell a little more fully upon this point of view regarding body and mind.

The Sexual Hormones in Relation to Body and Mind.—The sexual hormones (from *hormao*, I excite) which determine the mental and bodily characters of the two sexes are produced by special interstitial cells contained in the reproductive organs of the two sexes, and these hormone cells can and do functionally act independently of the germ cells. They exist prior to birth, and having determined the sex characters in the infant male, they soon disappear or pass into a resting stage until puberty, when they reappear and determine the secondary male sexual characters; a complete mental revolution then occurs and a vague longing, followed by an attraction to the opposite sex is determined by the sensitising influence of their internal secretion on the brain. If these cells are destroyed, sexual desire is lost. Many other facts could be quoted to show the profound influence of the internal secretions of the sex glands on mind and body. Another fact which speaks of the intimate relation of the sex organs to mind is the fact that a large proportion of the cases of true insanities or psychoses and psycho-neuroses commence at the times when the sex instinct matures and wanes.

The Endocrine Glands in Relation to Body and Mind.—Again the influence of the secretion of the thyroid gland on the development of the brain is shown by the fact that its absence in the infant is associated with cretinous idiocy. Administration of the gland permits the brain to grow and with it the mind develops. Older people, especially women at the change of life, suffer with a failure of secretion of this gland and a curiously characteristic bodily condition, known as myxoedema, occurs. With this there is a disappearance of the energy substance in the brain cells, and slowness of thought, slowness of speech, and frequently mental disorder. Administration of the gland restores the body and mind if it is not begun too late. Another ductless gland, which is no larger than a bean, seated in a little bony saddle (*sella turcica*) at the base of the skull, controls the growth of the body and is intimately associated with the reproductive organs. Still another gland, the suprarenal, contains a store of adrenalin which, when it is discharged into the circulation stimulates the sympathetic nerves; automatically, under the exciting influence of the emotions of fear and anger, this substance, so discharged, acts as a powerful defence mechanism in the instinct of self-preservation by causing a rise of the blood pressure, a mobilisation of sugar for the production of energy by the muscles for fight or flight, a stimulation of the heart's action, increase of the blood supply to the muscles, and increased coagulability of the blood, so that wounds are less likely to be fatal. Again, there is an intimate association between the development of the brain and the cortex adrenalis, also between this endocrine organ and the reproductive functions.

I might go on at great length showing the importance of these ductless glands and of the autonomic nervous system in relation to the primal instincts and emotions.

HABITS IN RELATION TO BODY AND MIND.

In daily life human beings are largely occupied in the performance of purposeful habits having their origin in the satisfaction of these primal instincts common to men and animals; they are acquired consciously by imitation or invention, but when perfected the will has merely to initiate the action and the sensorimotor reflex mechanism unconsciously carries on. It may be considered that in the subconscious mind there are a series of reflex patterns which when once started proceed in orderly sequence, the pattern of the last incoming sensory stimuli serving as the pattern of the next coördinating directing motor stimuli. The highest psychic level (consciousness) does not take any active part, but is watchful that the purpose willed is fulfilled; for it exhibits awareness when this series of reflex patterns is interrupted or inefficient. We know from experience how fear and apprehensive self-consciousness may interfere with the efficiency of any habitual action.

THE HERD INSTINCT AND HUMAN PROGRESS.

In proportion to the evolution of society and the progress of civilisation, the social instinct comes to dominate more and more human thought and behaviour. The bond of union whereby the members of the herd are willing to sacrifice individual interest and even life is the primal source of preservation for the herd, and to a certain extent therefore for its individual members. This instinct of the herd is, however, a device of Nature for the preservation of the species. It has played in man a predominant rôle in the evolution of language and abstract thought and the advance thereby of culture and civilisation. The habits, customs, and social usages of the herd dominate human life in thought and behaviour and they serve to control the instincts. Owing to over-population and crowding in cities there has arisen among highly civilised people an increasing tendency to a disharmony between social and physiological conditions regarding the sex instinct and its natural gratification. The correlation of body and mind is conclusively shown by the fact that a complete mental revolution peculiar to each sex occurs in adolescence and with it comes a new and great source of psycho-physical energy, the vital impulse to propagate which the social instinct impelled by the stress of self-preservation is enforced to control by contraceptive methods, or—using Freud's expression—to sublimate, that is, direct into other channels—e.g., religion, art, music, literature, and sport.

The social habits, customs, and usages of the herd were and are still too often based upon tradition and dogma connected with mysticism and beliefs in the supernatural, regarding body and mind and body and soul, and before biological science was illuminated by the theory of evolution, few people ventured to differ

from the herd regarding dualism. We now realise that in each individual life the furniture of the mind is the memory of the conscious and unconscious experiences and the bonds that united them. There can be no mind without memory and there can be no memory without body seeing that all psychic processes are dependent upon oxidation processes of a bio-chemical nature. We cannot separate psychical from physiological processes.

THE PERSONALITY IN RELATION TO DEEP FEELING AND EMOTION.

The Ego is aware of his individual personality by the continuum of subjective feelings arising from the whole body in its relation to its integral parts and as a whole to the external world. All experiences of the Ego, attended by deep feeling and emotional discharge, strike at the very roots of the three primal instincts and the physico-chemical changes therewith reverberate and reverberate in the preorganised emotive subconscious sensori-motor and vegetative systems. These nervous and bio-chemical preorganised mechanisms, which have progressively developed in the animal body as a result of evolution in the long procession of countless ages, have become endowed with a specific bio-rhythm attuned to the primitive self-conservative animal emotions—e.g., anger, fear, disgust, and the tender emotions connected with the sexual instinct. The sentiments and passions which are the outcome of the evolution and interaction of the primitive emotions with the established bonds of union of the herd are likewise endowed with a specific bio-rhythm. Consequently an experience with an intense emotional tone long after it has left the field of consciousness may be still operating subconsciously by the involuntary and unconscious bodily expression of the emotions exciting the associated subconscious memory of the emotional experience, and this in its turn reacts on the body. A vicious circle is thus established by which we may explain: (1) the perseveration of the hysterical derangements of mind and body caused by emotional shock; and (2) anxiety neuroses with a mental conflict involving a struggle between the instinct of self-preservation and the social instinct of the *amour propre*.

EMOTIONAL SHOCK AND WAR NEUROSES.

Hysterical disabilities afflicted a large percentage of the rank and file of the conscript armies in the Great War. The emotion of fear and the wish to escape an intolerable situation led by auto- and hetero-suggestion to various bodily defensive mechanisms, in the nature of hysterical paralyses, tremors, contractures, mutism, blindness, deafness, and their perseveration. These could be prevented largely by suggestion associated with good discipline, morale, and *esprit de corps*. It was found that the number of cases in a regiment increased enormously where these were absent.

Men who had long suffered with tremors, contractures, paralyses, mutism, and other disabilities which they had come to believe were permanent were sent to me and were cured in a few minutes, a few hours, or a few days by various modes of contra-suggestion and persuasion, and when cured it was astonishing how completely changed was their mental attitude: the trembling, the cold blue hands and feet, the sweating and the anxious facial expression—all signs of the emotion of fear—disappeared upon the bodily recovery and the breaking of the vicious circle. About 95 per cent. of the cases of so-called "shell-shock" were really emotional shock, and only 5 per cent. were due to commotional disturbance produced by proximity to the explosion of a large shell. These were the true shell-shock cases, and if not immediately fatal they recovered as a rule much quicker than the emotional case, for the emotion of fear and the unconscious wish to escape from an intolerable situation was not usually a part of their mental attitude as a soldier.

Officers seldom suffered with these hysterical disabilities which were so common in the men; their nervous disability was usually an anxiety neurosis in which the instinct of self-preservation did not play such a dominant part as it did among the rank and file. An exhausted, irritable nervous system, associated with various forms of bodily derangement—e.g., headache, insomnia, tremors, and disorders affecting one or other of the following systems: cardiac, vasomotor, respiratory, digestive, genital, and glandular—was the result of a mental conflict in the conscious and the subconscious mind between two primal instincts—self-preservation and the esteem of the herd. In some the fear of death played the more important part. In others it was an altruistic fear connected with responsibility for the lives of the men under their charge, rather than their own self-preservation, which led to the nervous breakdown. Most of those officers who suffered with an anxiety neurosis were troubled with terrifying dreams of their battle experiences; some suffered with a recurring dream in which they lived over again some horrifying or terrifying experience, so vividly that they were afraid to sleep. Some were unable to recall their dreams, but the mental and bodily depression on awaking showed that they had been dreaming of past painful experiences. Many shouted out in their sleep commands to their men, and a few fought or walked in their sleep. The war has shown the great importance of the subconscious mind; but experience has demonstrated the fallacy of the Freudian doctrine that all dreams with fear are related to forgotten sexual experiences causing a mental trauma. Moreover, it has shown that individual self-preservation and a mental conflict arising from fear, associated with this primal instinct, suppresses sexual desire. It is interesting to recall that Shakespeare in Mercutio's description of "Queen Mab" refers to soldiers' dreams; and in Lady Percy's speech to Hotspur attention is drawn to the mental conflict in Hotspur's mind and its interference with his marital duties.

But an individual suffering with an anxiety neurosis, which has its origin in the fear that he has irretrievably lost the esteem of his fellows, may arouse through the herd instinct bodily and mental effects similar to those produced by fear for self-preservation. This fact may be explained by the two instincts having been by evolution attuned to a corresponding specific bio-rhythm in respect to fear.

EVOLUTIONAL LEVELS.

We cannot leave this subject of body and mind without a consideration of the doctrine of Hughlings Jackson's levels. We may consider that there are three evolutionary levels in the nervous system, and this hypothesis is supported by comparative anatomy and the effects of functional and organic disease of the nervous system. The lowest level is present in all animals and subserves the primal instincts of self-preservation and preservation of the species; it consists of two parts: (1) The vegetative nervous system, consisting of two systems (*a*) the involuntary autonomic or parasympathetic, and (*b*) the sympathetic, with which are associated the ductless glands, and which controls and directs the bodily needs and functions concerned with gratification of the appetites and desires connected with the instincts of self-preservation and propagation; (2) the protopathic sensorimotor nervous system which controls the reflex activities for protection against pain and injury, including injurious degrees of heat and cold.

The second level is the discriminative sensorimotor level. In the vertebrate series we find two great groups: (*a*) Macrosmatic, in which the nervous structures that are especially developed are those connected with smell and taste; and (*b*) microsmatic, in which the senses of sight, hearing, and touch are especially developed. The archicortex of the cerebral hemispheres is highly developed in the former, the neo-cortex in the latter. The projection centres of these senses are around the primary fissures.

The third highest level is the psychic level in which there is a great development of the cortex of the brain, and which in man far exceeds in development that of the largest anthropoid apes. *Pari passu* with this great development of the cerebral hemispheres is a bodily development far surpassing in excellence all the lower animals—viz., erect posture—by which the forelimbs are no longer used for progression; and perfection of the hand, whereby it becomes not only the instrument but the instructor of the mind, for guided by vision it is enabled to create and make the most varied mental adjustments to environment and control the forces of nature. By the creation of graphic and articulate language, which have simultaneously progressed, has been built up a great social heritage constituting an endowment to civilised man, whose organ of mind is, however, no larger or heavier, and possibly potentially no better, than that of the man who dwelt in caves 50,000 years ago—

whose only common mode of expression was, it may be conjectured, mainly by vocal sounds, gestures, and facial expression, a primitive, universal, emotional language understood by all peoples.

ANATOMICAL SUBSTRATUM OF THE PSYCHIC LEVEL.

Now, in idiots who are incapable of articulate expression and abstract thought we find only the two lower levels properly represented, the development of the anatomical basis of the psychic level—i.e., the millions of cells in the cortex—is arrested in development and we have a condition then of amentia or absence of mind. If we examined sections of the cortex we should find the supragranular layer of pyramids especially affected. This layer, as Bolton has shown, is developed later than the infra-granular layer. Moreover, I have shown that as you rise in the zoological scale of vertebrates, it is this layer which increases in depth and number of cells.

Simple dementia or loss of mind may be associated with a limited destruction of the anatomical basis of mind—viz., the highest psychic level—and, the two lower levels being more or less intact, the habitual acquired sensorimotor reactions may remain and the individual then may behave as an automaton in response to environmental influences and bodily needs. Every part of the body is represented in all the three evolutionary levels and, as Hughlings Jackson taught, the last to come evolutionally is the first to go. The three physiological levels are functionally interdependent. The highest level, upon which awareness and volition depend, is able to act through the second discriminative sensorimotor level to alterations in the streams of sensation coming from the external world; while the third and lowest level evolutionally is concerned with the involuntary vital functions of the body, and therefore constitutes the basic source of the desires and impulses connected with self-preservation and propagation. I have endeavoured in this address to show the inseparability of body and mind, and the importance of the study of biology and bio-chemistry in the study of mind in health and disease.

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Croonian Lectures
ON
**THE OBJECTIVE STUDY OF
NEUROSIS.**

*Delivered on June 9th, 14th, 16th, 21st, before the
Royal College of Physicians of London.*

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LECTURE I.

IN this series of lectures I propose to deal with certain types of movement that are the manifestations of those phases of cerebral activity which have been generally considered to be confined to molecular changes in the cerebral cortex and its great ganglia. I refer to processes of thought and feeling. The modern knowledge of the functions of the brain has led us to look to this organ almost exclusively for the manifestations of mental activity; we are apt to forget that to such a great psychologist as Aristotle the brain was nothing but a mass of cold matter whose function was to cool the blood coming from the heart and lungs, serving only as an intermediary link between the organs of sight, smell, and hearing, and the heart where their sensations were perceived. It is through our concentration on the cerebral aspect of mental activity that we have been so slow to realise that the body partakes in the movements that express this activity and, by ignoring these bodily signs, the possibility of establishing an objective standard in our interpretation of neurotic disturbance is, to a great extent, lost. What, then, are data furnished by objective observation of the activity of the nervous system? I cannot do better than quote the views of Bergson as summarised by Hoffding: "All that takes place in the surrounding world and in my own body, including my brain and nervous system, consists only of movements of different kinds and degrees. From the external world movement is spread abroad through our body. It reaches the spinal column and the brain by way of the sense organs and the nerves, and proceeds into peripheral movements. Our body is an instrument which receives movement from the outside, and restores it to the external world. There is not from this point of view any difference between the brain and other parts of the body. The brain is merely stronger than the other organs in preserving the action that it has thus received, and does not always reproduce

them in movement immediately but often makes them coöperate in ulterior movements. The body, including the brain, is an instrument of movement and nothing else. To no degree, in no sense, from no point of view, does it serve to prepare and still less to explain a representation. That which, in our perceptions, can be explained by the action of the brain, includes the actions which are commenced or prepared or occasioned, but not our perceptions themselves. Still less does the activity of the brain comprise any explanation of memory and of higher mental activity. If everything in the brain and outside is movement we must not look for anything else than what is observable. The nervous system has only physical properties, and has no other power than that of receiving, preserving, and continuing movement. Movement alone is sensible to us and movement can produce nothing but movement. The whole effect of physical processes is exhausted by the effort of motive adaptation (*le travail d'adaptation motrice*). If the brain is ill, it is only movements and nothing else that are arrested." No scientific worker is likely to quarrel with this view, but it is important to realise that its adoption leaves us untrammelled by any metaphysical implications; it is as consistent with materialism as with idealism, with monism as with dualism.

RELATION OF PSYCHOLOGY TO PHYSIOLOGY.

It will be plain that a psychology founded on this objective basis leaves untouched all that constitutes for us the chief interest in life. In terms of objective psychology such expressions as meaning and purpose can find no place; by severing it from teleology, history, from the point of view of the psychologist, will become unintelligible. This was, indeed, the view of psychology held by Münsterberg, who argued that the sole function of psychology is to provide us with mechanical uniformities of sequence by the aid whereof to calculate the future behaviour of our fellows in so far as it is not modified by fresh purposive initiative, and that the whole of psychology is a temporary stop-gap, by which we eke out our defective physiology, but which must sooner or later cease to be of use, and therefore cease to exist, as physiology advances. Indeed, to such a pitch must psychology necessarily be brought, if we listen to the warnings of Avernarius on the besetting sin of "introjection."

Now this may or may not be a desirable state of affairs for the psychologist, but I maintain that for us as physicians it is the only possible. The late Dr. Mercier entitled his text-book of insanity "Disorders of Conduct," for of mind he said he knew nothing. It may, indeed, be held with some plausibility that there are no such things as disorders of mind. As physicians we are confronted with cases exhibiting disorders of conduct—that is, of the mechanism of expression, and our psychology must stand in exactly the same relation to mechanism as does our physical science. It is necessary to insist on these

methodological points because we find both neurology and, to a lesser degree, physiology in a state of great confusion owing to their non-observance. Consider the mess that neurology has made of the subject of aphasia, by a careless use of physiological and metaphysical concepts. It arose merely because neurologists talked of memory—a non-physical entity—being stored up in nerve cells without realising that they were talking nonsense. All that they were really entitled to say is that the mechanism of representation is preserved in certain neurones.

PHYSICAL DISTURBANCES THE PRIMARY FACTOR IN THE NEUROSES.

Thanks to the labours of Pierre Marie, and in more recent times to those of Head, we are slowly reconstituting our knowledge of aphasia as being in all its forms a disorder of the mechanisms of expression. It is interesting to note that we have only now arrived at the same conclusion on the subject of aphasia as that advanced by a philosopher, M. Bergson, nearly 30 years ago, as soon as he detected the confusion of thought that lay at the root of our difficulties. It is from much the same causes that so much confusion arises in physiological literature on the subject of sensation—that is, from the incautious use of non-physical terms in the description of physical states. The point of view that I am about to deal with in these lectures has for its object an attempt to define in objective terms the chief data that may lead us ultimately to formulate the nature of the physical disturbance of mechanism that constitutes the primary factor in the neuroses. That such a physical disturbance is the cause of the neuropathic condition and precedes its manifestation I hold very strongly. One fact emerges from all the investigations that have been conducted in recent years by the methods of analytical psychology, and that is that in the vast majority of cases the experiences of the neurotic differ in no way from those that fall to the lot of ordinary healthy men. The data furnished by the war are often cited as an argument to the contrary, but I think that they really furnish irrefutable evidence that an organic disturbance or failure of organic equilibrium preceded the manifestation of the neurotic symptoms and could not have been caused, however much it may have been aggravated, by the individual experiences. In the armies of the Allies and those of the enemy millions of men were exposed to similar conditions, yet only a small number were brought to our hospitals suffering from a neurosis. Doubtless all of us who were in the line showed for a longer or shorter period the disturbances due to fatigue or functional hypertrophy of certain nervous mechanisms, but only those succumbed who were organically unsound. Sir Frederick Mott was able to obtain a history of pre-existing neurotic symptoms in 80 per cent. of the cases of soldiers under his care for neurotic disorders. But the point hardly needs pressing; had those who have contributed to the literature of the war neuroses

been permitted to undertake regimental duty in the line, thus to know their men, as one only can do by constant contact, they would have found little difficulty in spotting the future cases of neurosis before ever a shot was fired. Were these cases of organic nervous weakness the victims of infantile and childhood experiences that left an indelible mark on their nervous constitution? There is no reason to suppose that as a whole their experiences differed from those of the average child of their particular social milieu. We are, I think, justified in assuming that an organic disability exists as an antecedent to every neurosis, and in employing methods for objective evaluation of organic efficiency in looking for it.

STUDY OF CONDUCT AND OF SPECIFIC REACTION OR MOVEMENT.

Such an objective study must necessarily be conducted along many lines of observation; but, broadly speaking, there are two methods at our disposal—the study of conduct and the study of specific bodily reactions or movements.

The study of conduct is a purely objective study of all those activities which collectively represent to us all that we can know by observation of the exterior aspect of life. The study of movements is supplementary to the study of conduct. By movement we understand not only the manifest muscular reactions, but also secretory and circulatory responses. The study of conduct in a search for signs pointing to definite organic disorders must of necessity furnish much evidence that is ambiguous and much that is definitely misleading. The recognition of the actuality of our own and our fellow men's life of unique and incommunicable feeling compels us to admit the existence of much that from its incommunicable nature falls outside the sphere of physical reality. The weakness of any objective study of conduct is that much of our information depends on verbal communications from the subject studied.

Now, quite apart from this unique incommunicable aspect of experience, there are a host of affective states and sensory experiences that we have to a great extent in common and that we find the greatest difficulty in communicating. Language is in its essence a method of communication evolved solely in response to practical needs—that is, for the communication of information essential to the maintenance of our social life. The communication of the greater part of our experience serves no such useful purpose, and hence has never acted as a stimulus for the evolution of appropriate language. Those of us who are musicians know that we have a whole range of experience which in its broader aspects we have no reason to suppose to be unique, but which for all that remains practically incommunicable. It is the function of the artist to bridge this gap in our social life by presenting his immediate intuition of reality, but we all know how rarely and how imperfectly art succeeds. It is precisely for this reason that the study of those

movements which are the exterior signs of states of feeling becomes so important. When our methods of observation become sufficiently perfected we may be able to check by means of these stereotyped forms of reaction the deductions that we draw from the concerted actions, words, and silences of our patients.

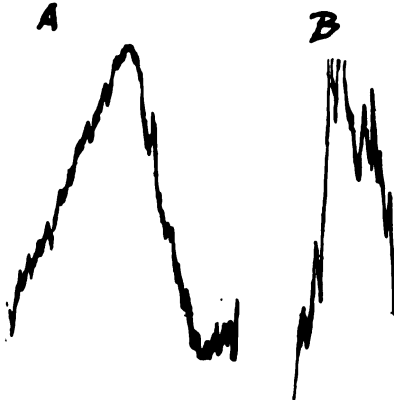
TYPES OF MOVEMENT STUDIED.

The movements which I propose to study are of two types—those which are the exterior manifestations of the specialised response of certain nervous mechanisms, and those which connote the generalised reaction of the body as a whole to stimuli which disturb or threaten the unity of vital action. With movements of the first type we may deal briefly, because their disturbances belong rather to the category of what are known as organic nervous diseases than to that of the neuroses. When we speak and at the same time press the hand on the throat we become aware of movements of the larynx which are easily palpable. They are still more pronounced when we sing, and by pressing the nail of the index finger on the free edge of the upper border of the thyroid cartilage we may readily feel the cartilage move upwards higher and higher with each ascending note of an octave and descend by similar steps as we go down the scale. These movements may be recorded if we fix to the neck a firm leather collar supporting a small spring, one end of which presses downwards on the cartilage and the other is fixed to the collar. At right angles from the spring a small button is soldered which impinges on the drum of an air capsule conveniently attached to the collar. The vibrations of the tambour membrane are conveyed by a rubber tube to another tambour fixed on a stand and this in turn actuates an optical lever on which a beam of light is projected. The magnified excursions of the optical lever are recorded photographically.

Fig. 1, A, is a record of the movements of the cartilage in singing up and down an octave. Now, if instead of singing audibly I think of the notes of the octave, and at the same time record the laryngeal movements, I shall obtain a similar picture (Fig. 1, B). The movements are

generally smaller than in actual singing, and for purposes of comparison they have been roughly magnified three times in this figure by moving the recording cylinder further away from the optical lever.

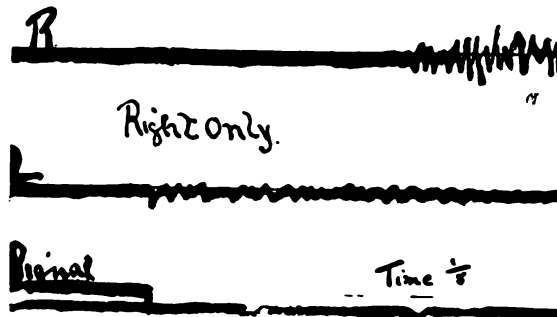
FIG. 1.



THOUGHT A MODE OF MOVEMENT, WHETHER
VOCALISED OR SILENT.

Thought is expressed either by external or internal speech, and whether the speech be externalised or internal it is a mode of movement. If I recite to myself a speech or a poem I can demonstrate the occurrence of similar laryngeal movements, though in this case their relation to the corresponding speech movements cannot be demonstrated with the same ease. Now to think of the notes of an octave or to recite a poem silently is not quite the same thing as to sit quietly and think over any problem or make arrangements for the future. In the first case we are trying to represent to ourselves every tonal step of the octave and every word of the poem, whereas in the latter we are not so concerned with the verbal niceties of our problem as with the conclusions to which it leads. Our motor manifestations in the second case will be more sketchy, the hint of the beginning of a word movement will be sufficient to convey to us the sensory impression of the word just as in reading psychological experiments have shown that the eye does not move along the line of print from

FIG. 2.



letter to letter ; but that in a series of jerky movements, it seizes sufficient letters to allow of the recognition of any one word and then darts on to the next. The motor manifestations constitute what Ribot has happily termed the skeleton of our presentations. What, then, fills in the skeleton outlines ? The answer varies for each individual. Ask a number of men to think of a given multiplication sum—some of them will see the figures, others will hear them, others will combine a feeble visualisation with a certain sense of movement, feeling as if the eye were travelling down a row of figures and each were visualised in turn in its place. Those who manifest most markedly laryngeal movement probably fill in the gaps of the skeleton with kinæsthetic representations of the vocal movements that do not actualise. The rôle of actual speech movements in representation is probably under-estimated. Had I been asked some years ago before I had considered the question in what way I represented to myself the octave I should have answered unhesitatingly that I heard it, I have

now little doubt but that my laryngeal movements are the first link in evoking the ultimate auditory representation, because though I am told that I have a fairly good ear, my musical memory is to a great extent limited to the representation of those notes that lie in the compass of my voice. Similarly, in visual representation our visual images appear to be to a great extent stimulated by kinæsthetic images arising from the centres for movements of the eye muscles and in extreme cases the stimulation of the motor cell may translate itself into actual movement. I have often performed the experiment of asking an unsophisticated subject to describe to me Trafalgar Square as he would see it if he stood at the base of the Charles I.'s monument. If one is careful to avoid standing exactly face to face, and thus allowing him to fix his eyes on the observer's, in nine cases out of ten I find that as he reels off the series of objects to be seen his eyes move from the right when he mentions Morley's Hotel, to the left when he comes to the Union Club, and upwards as he describes the Nelson monument. It is not only in the mechanism of internal speech that we find these movements, but in the preparation for action. Figs. 3 and 4 represent the results I obtained in some experiments in which the subject was asked to dorsiflex both hands the moment he heard a sound signal. Both forearms were lying with the palms downwards on the table and the extensor group of each forearm was connected to two galvanometers which were constituted by two of the loops in an oscillograph. In the case illustrated the patient was a left-handed man, and in the experiment recorded in Fig. 2 he was asked to raise the right hand only when the signal sounded. It will be observed that from the time that the signal sounded till the actual moment that the right hand was raised there was a well-marked electrical vibration observable in the extensor group of the left arm. The idea of movement in this subject was represented by an actual activation of the muscles, and as he thought of all his movements primarily in terms of the left hand, it was the left extensors that responded. When he was asked to dorsiflex both hands simultaneously, we again see the representation of movement in the left hand (Fig. 3). On asking him to move the left hand alone, the same left-sided representation occurred (Fig. 4). It appears that this connoted the idea of movement on which he was concentrating, and was not in any way a preparatory performance, since the latent times of moving the left hand alone and the right hand alone were identical. In a right-handed subject the phenomenon was reversed. It is of interest to note that for reasons that I shall deal with when we come to talk of tonus one can be sure that this motor representation was of the nature of a voluntary muscular contraction, not an increase of muscle tonus. This motor representation has its influence on all our forms of thought. A very cursory survey of the expressions that we use, whether in the language of description or of abstract reasoning, is enough to show that a dynamic symbolism is universal.

Some time ago Binet made some observations on chess players who were able to play several games blindfold and simultaneously. We should anticipate that such men had an abnormally acute power of visual representation; but though they all stated that they could without much difficulty visualise the chess-board, they agreed that in actual play they never did so, and that visualisation would, if anything,

FIG. 3.

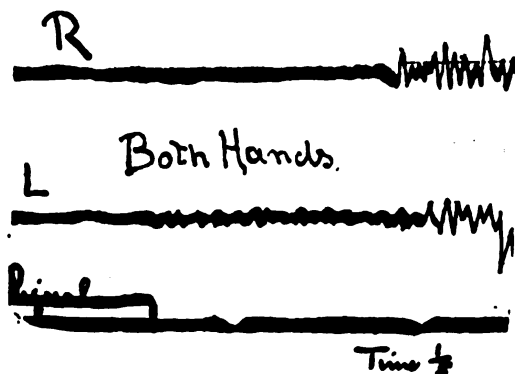
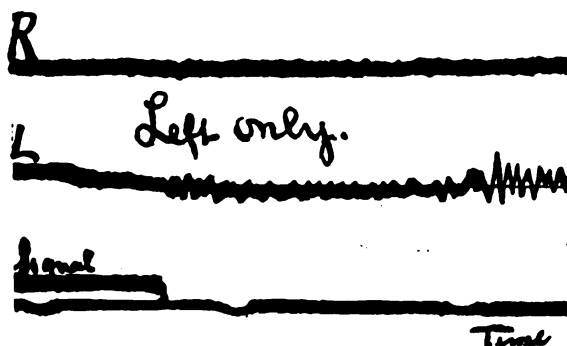


FIG. 4.



rather impede than help them. The chessboard to them was represented in dynamic terms as a congeries of contending forces. A knight was a force acting diagonally and a rook vertically. I do not intend to pursue the subject of these specific forms of motor reactions further, because, as I said before, their disturbances belong more appropriately to the study of gross organic lesions; but it must not be assumed that the specific mechanism by which representations normally occur is without influence on the symptomatology of the organic disturbance which, I hope to show, underlies the neuroses. As to the nature of this influence on conduct I will confine myself to one

hint. A surgeon with world-wide experience of the congenitally blind once told me that when a blind man was vicious his abnormality often assumed forms more gross and detestable than occur among the sane with normal eyesight. I have the impression that men with a predominantly auditory type of representation are less nice about physical matters than those with a predominantly visual type, and that the visualist is less nice about the choice of words and less prone to take umbrage at a harsh expression than is the auditive.

CONNEXION OF MUSCULAR TENSION WITH INTELLECTUAL OR PHYSICAL EFFORT.

I next propose to deal with those movements that connote a generalised reaction of the organism, from the study of which I think we can gain much information as to the fundamental disturbances of mechanism in the neuroses. In the first place I will invite you to study those organic reactions by which the body responds as a whole to stimuli occasioned by the vigorous activity of some specific mechanism. To denote this form of response I prefer to avoid any terms that have subjective implications, such as attention and conation. I shall therefore speak of this type of reaction as effort, and distinguish for purely methodological reasons intellectual and physical effort.

That effort is accompanied by some general alteration of muscular tension has been generally appreciated in a vague fashion, but I have found no record of any attempt to measure and determine the nature of these alterations. Now, there is a very simple and homely method by which the alterations of tension in the quadriceps muscle can be verified. Everyone has at some time or other noticed that when the legs are crossed in such fashion as to allow the crossing leg to hang almost freely downwards the foot can be observed to pulsate up and down with every beat of the pulse; the lower leg, in fact, constitutes the lever of a sphygmograph. If when the legs are so adjusted as to show the pulsation and we are reclining comfortably in an armchair in front of a tiled fireplace we carefully observe the height of the pulsating toecap against the line of intersection of the tiles, we can readily verify any change in the level of the foot. Now, still keeping the eye on the alignment between the toecap and the crevice in the tiles, make some voluntary effort—either attempt to perform some difficult piece of mental arithmetic or grip some object with all your force. It will be seen that coincidently with the effort there has been an appreciable upward movement of the foot—that is, a shortening of the extensor muscles of the thigh has occurred. It is quite easy to measure this shortening and to determine its nature. To do so, it is above all necessary to ensure that the crossing leg is completely relaxed and that the lower extremity is hanging sufficiently freely to exert a constant pull on the quadriceps tendon. This state is present

when the foot can be observed to be pulsating vigorously with each heart beat, and is brought about by taking care that the free suspension is in no wise interfered with by the underlying knee supporting the calf muscles. The knee of the crossed leg should lie in the upper part of the popliteal space of the crossing leg. The toecap of the shoe is then attached by a thread to a suitably placed lever whose excursions are recorded on the kymograph. A shortening of the quadriceps and upward movement of the foot will be recorded by a downward movement of the lever. Fig. 5 is a record of the quadriceps shortening manifested in one type of effort, the solving of a problem

FIG. 5.

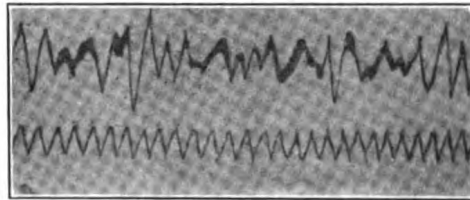


The upper tracing is that of the movements of the foot. A downward movement of the lever indicates an upward movement of the foot. The lower tracing is that of the respiration. Time in seconds. Thick black line indicates approximate duration of stimulus—a multiplication.

in mental arithmetic. It is now necessary to inquire into the nature of this contraction of the quadriceps; is it of the nature of a so-called voluntary contraction—that is to say, produced by direct cortical innervation, or is it due to an increase of postural tonus? The work of Wertheim Salomonson has shown that it is possible to differentiate between these two types of muscular contraction. It was shown by Piper that the electromyogram of a voluntary contraction as recorded by the string galvanometer is manifested by an irregular oscillation having the frequency of roughly 50 vibrations per second. These vibrations were considered by Piper to indicate the number of motor nerve impulses reaching the muscle in a second. It is for many reasons certain that they really indicate nothing of the sort, but they served Salomonson to differentiate a voluntary muscular contraction from a tonic contraction which he proved to be entirely innocent of these vibrations. Fig. 6 represents a record taken by the Bock Thoma oscillograph of the vibrations occurring during a voluntary contraction of the quadriceps. In order to investigate the nature of the quadriceps contraction in effort, I recorded simultaneously the movements of a lever connected with the toecap and the electromyogram obtained by

a string galvanometer connected with needle electrodes plunged into the substance of the quadriceps muscle. During the effort contraction produced by a dynamometer squeeze it will be seen that there is no trace of the Piper vibration, and we are entitled to speak

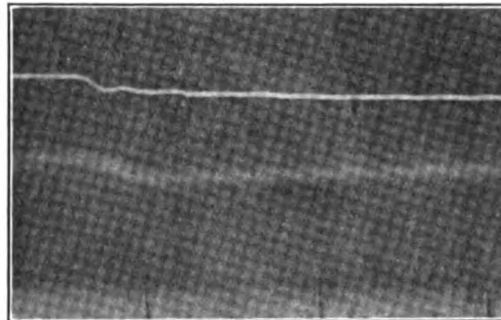
FIG. 6.



Electromyogram of a voluntary contraction.
Below time in 0.01 secs.

of the effort phenomenon as a tonic contraction (Fig. 7). The electromyogram is, moreover, of some considerable interest, as it shows a phenomenon that I have verified in all my records of tonic contractions—at the commencement of the tonic contraction, as evidenced by the movement of the lever, there is a current of action of the order of about 0.1 millivolt. The current of action is of much longer duration than the diphasic variation of a single muscle twitch. Its duration is about 0.4 sec. It will be noted that after it has subsided the galvanometer registers a

FIG. 7.



Upper line is that of movements of foot. Downward movement of lever indicates an upward movement of foot. Lower line is the shadow of galvanometer string. Time in $\frac{1}{5}$ seconds.

perfectly straight line in the position of rest, although the lever registers a continuance of the tonic contraction. It is of some importance to know the nature of the nervous mechanism responsible for this reflex, and this, unfortunately, must at present remain a matter of great uncertainty. Boeke has

found in voluntary muscles nerve endings which appear to be of sympathetic origin, and there is some reason to believe that the centrifugal path of the tonic reflexes is guided by sympathetic fibres; but in spite of the suggestive work of De Boer the question must be regarded as still open. I have found this tonic effort reflex much increased in cases of unilateral pyramidal lesions on the affected side and very much diminished, but still quite definite in cases of tabes. In a case of cerebellar tumour with very marked unilateral hypotonus placed at my disposal by my colleague, Dr. J. S. Collier, the effort reflex was absent on the hypotonic side and normal on the sound side. In the case of the flexed knee, it appears that the tonus of the extensor group is alone increased, while that of the flexor muscles, which by virtue of the position of the leg are already in a state of greater tonus than the extensors, is unaffected or diminished. It is of some interest to determine whether this distribution of tonic innervation occurs elsewhere. If the forearm be flexed at the elbow and supported on a block, and the completely relaxed hand be allowed to hang over the end of the block in a position of supination, it is easy to obtain a record of the hand movements by attaching the lever thread to the head of the middle metacarpal by a pellet of wax. In such a case it will be found that dorsiflexion of the hand occurs in response to effort, whilst when the hand

FIG. 8.



Tracings of A, tonus reflex of flexor; B, of extensor muscles of wrist during mental effort. A downward movement of the lever indicates an upward movement of the hand.

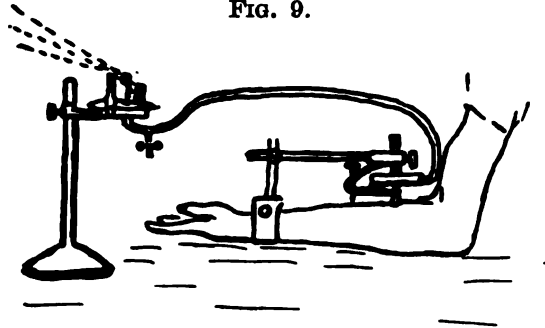
is supinated and allowed to fall backwards over the edge of the block a flexion of the hand at the wrist results (Fig. 8, A and B).

In the case of the elbow-joint, which like the knee-joint only permits movement through one half of a circle, the tonic effort reflex may be demonstrated in the triceps when the upper arm is supported at right angles to the body and the lower arm is allowed to hang downwards. The tonic effort reflex, as shown by the wrist-joint experiments, only affects those muscles which are in a stretched condition. I will next consider what happens when the limb is in a position in which the tonus of the antagonistic groups of muscles is presumably equal. To investigate this point it was obvious that movements of the extremities could no longer serve as indicators; it was therefore necessary to devise some method for the direct measurement of alterations of muscle tonus.

MEASUREMENTS OF ALTERATIONS OF MUSCLE TONUS.

It is obvious that for this purpose the registering apparatus must not vary its position in relation to the muscles of the limb, as otherwise a slight involuntary shifting of the limb would be interpreted as an alteration of muscle tonus. To secure this end, in the case of the forearm a suitably devised clamp was fastened firmly to the bony prominences formed by the heads of the radius and ulna. From the clamp a light rod projected backwards to hold a tambour, with a spring attachment that controlled the pressure, with which a short rod was pressed into the flesh over the belly of the muscle to be investigated. The free end of the rod was in contact with the centre of the tambour membrane. Any increase of the tonus of the muscle would press up the rod, and the resultant air displacement in the tambour was conducted by a tube to a delicate Marey tambour fixed on a stand. In place of the ordinary writing lever over this capsule an optical lever was substituted, consisting

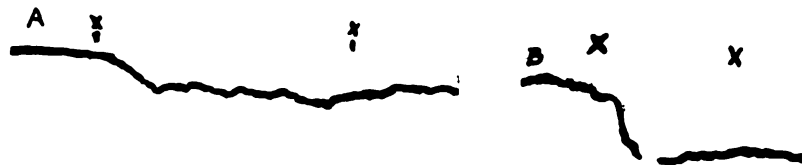
FIG. 9.



of a light mirror fastened to the middle of a piece of silk stretched immediately above the tambour. From the back of the mirror projected a short lever 2 mm. in length, actuated by a short reed projecting from the middle of the tambour membrane. By such an arrangement the air displacement, due to movements of the rod resting on the muscle, could be magnified to any desired extent, and a similar apparatus attached to the antagonist muscles allowed simultaneous records of the alterations of tonus to be taken (Fig. 9). The photographic records (Fig. 10) show that with the wrist-joint in the neutral position there is a simultaneous increase of tonus in both antagonistic groups of muscles of the forearm. Similar records have been obtained from the majority of the more accessible skeletal muscles. The effort reflex appears to increase the tonus of all those muscles that are in a stretched or a neutral state. Fig. 11 is a photographic record of the increase of tonus during an attempt to say the "thirteen times" multiplication table. The subject was a very poor arithmetician; the first three or four stages were rattled off with ease and no increase of tonus appeared, but as the difficulty of the multiplication increased the effort showed itself in a gradual

increase of the muscle tonus. I have many records that show a similar correspondence between the degree of tonus and the intensity of the effort put forth, and we shall see later that in certain neurotics who are incapable of prolonged or intense effort the tonus reflex is correspondingly affected. Now as to the significance of the reflex—I have a very strong aversion to all forms of teleological explanations not confirmed by direct observation. One result of the increase of tonus is, however, fairly obvious. The influence of muscular and mental effort in increasing

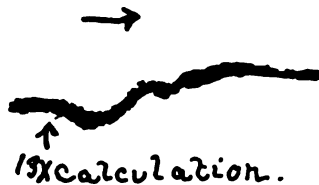
FIG. 10.



A, increase of tonus in flexors of wrist. B, increase of tonus in extensors.
Stimulus between x — x — calculation.

the tendon reflex response is universally admitted, though the current explanation that finds acceptance among neurologists is very unsatisfactory. We are always told that in consequence of the voluntary effort the inhibitory power exercised over the tendon reflex arc by the cortex is relaxed, and hence the response is increased. We know, however, from clinical evidence that the magnitude of the tendon reflex varies directly with the degree of tonus, and I have shown that one sign of effort is an increase of muscular tonus. In order to obtain an exact comparison of any two reflexes it is necessary that the

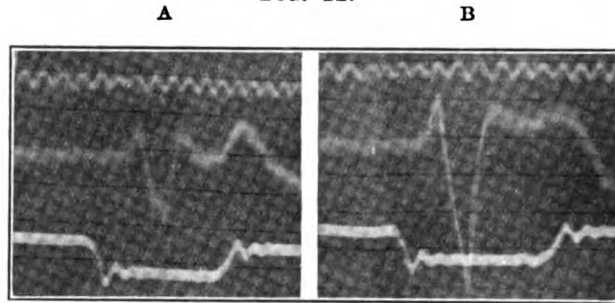
FIG. 11.



stimuli should be of equal magnitude. I constructed a pendulum hammer which when released at the same angle could be trusted to hit the patellar tendon with uniform force. The moment of occurrence of the stimulus was indicated by the hammer closing an electrical circuit which actuated a Deprez signal when it struck a piece of metal foil that was pasted on to the patella. Fig. 12 shows the tendon reflex at rest and during effort. It will be noted that in addition to an increased response during effort there is a

shortening of the latent period from 20σ to 15σ . This shortening of the latent period presents some difficulty as to its interpretation. If we assume with Piper that the velocity of a nerve impulse is 120 metres per second, and with Jolly and Hoffman that the latent period of the receptor organs and that of the muscle is about 11σ , we obtain values for the synaptic time lost in the cord of about 4σ . Now, the shortening of the latent period in the second of these two reflexes is of such a magnitude that it is very

FIG. 12.



Upper record is the electro-myogram of the knee-jerk, elicited A, when resting; B, when engaged in muscular effort. Lower record is the signal. Time in 1/100th of a second.

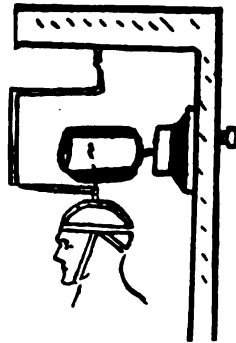
difficult to ascribe it to a diminution of the lost time in the central nervous system, and the same remark applies to the effector muscle and the receptor nerve-endings. Even if we consider that the diminution is spread over all three, its magnitude is very great in comparison to the total time involved. There is no reason to suspect the measurement of the velocity of the nerve impulse of any marked degree of inaccuracy, because it is confirmed by the comparison of the latent periods of the achilles tendon reflex and the knee-jerk in the same individual when the increased length of the latent period in the first reflex corresponds to the additional nerve tract traversed. I have found similar concordant differences in measuring the latent period of the triceps-jerk and the knee-jerk in the baby. Whatever be the explanation, the effort tonus reflex appears to be associated with an increased velocity of response as well as an increase of magnitude, in as far as these simpler reflex mechanisms are concerned. While the diffuse tonic reflex that we have been discussing tends to cause extension of the limbs, the position of the head in effort is differently affected.

EFFORT AND HEAD MOVEMENTS.

To study the head movements the subject was seated in a high-backed chair and to the vertex of a wire skeleton skull cap the free end of a piece of wire was connected by allowing it to lie loosely in a small brass tube soldered on to the vertex. The other end of the wire was fixed in a freely moving ball-and-socket joint on a wooden support fixed directly over the

head. The wire was so curved as to allow a small recording drum to be at right angles to its axis, so that a writing point fixed to the wire immediately above its joint with the skull cap wrote directly on the smoked surface of the drum (Fig. 13). With this arrangement the only head movements that can be recorded are those which take place at right angles

FIG. 13.



to the direction in which the drum is revolving. With this rather primitive instrument I had to obtain two successive records of the response to the same type of stimulus in order to obtain the resultant head movements. I soon found, however, that the lateral movements of the head are of irregular nature and bear no relation to effort. When, however, an effort, whether muscular or intellectual, is made there is a slight but definite forward movement of the head which lasts for the duration of the effort. The

absence of the vibratory action currents characteristic of voluntary contraction in the sterno-mastoids has led me to consider this movement to be tonic in nature, but the difficulty of exploring the small flexor muscles of the head will not allow of dogmatic statement. The bowed head observable in certain people when thinking deeply is obviously an exaggeration of this reflex.

EFFORT AND RESPIRATORY MOVEMENTS.

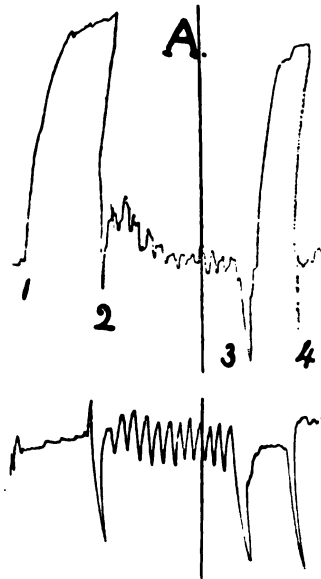
The relation of the respiratory movements to effort has long been known, and a series of observers have studied the alterations of the respiratory curve in the hope of finding distinctions typical of different mental states. Time does not allow me to criticise these records in detail; I can only subscribe to the generally expressed want of faith in the existence of special types of respiratory curve associated with specific mental states. There is, however, one factor on which everybody is agreed, and that is the reduction of the amplitude of the respiratory movements associated with effort. The usual method of observing respiratory changes by recording the movements of the thorax and abdomen is, however, inconvenient. The apparatus concentrates the attention of the patient on his respiration, and the net effect of the respiratory movements on intrathoracic pressure can only be estimated by the correlation of thoracic and abdominal tracings. In fact, one observer, Rehwoldt, uses no less than five tambours placed on different portions of the thorax and abdomen. The method I have adopted allows the total respiratory variation to be estimated with a minimal amount of disturbance to the subject. A soft rubber No. 1 catheter tube is fixed to the upper lip by a piece of plaster so that its free end is on the same plane as the aperture of the nostril. The tube is connected

with a Marey tambour and the pressure alterations in its air column caused by inspiration and expiration are recorded. After the first few minutes the subject is almost unaware of the presence of the apparatus, whereas the knowledge that the chest wall is influencing a tambour applied to it produces a curious concentration on the respiratory movements that as a matter of personal experience I have never been able quite to eliminate. The net results of the effect of effort on the respiratory movement are shown in Fig. 5 with a simultaneous record of the quadriceps tonus. The tidal air is reduced to a minimum and the respiration is slowed. We are all aware that when we attempt to perform any very delicate manipulation or some particularly exacting calculation we have a sensation of holding the breath and that the termination of a short effort of this description is followed by a prolonged expiration—a sigh of relief. Some years ago, when I conducted some researches on the phagocytosis of carborundum particles under different conditions, I found that the respiratory reaction during the performance of counting the particles ingested in a number of leucocytes was the most irksome part of the proceedings. This flattening of the respiratory curve is not to be attributed to a simple diminution of the respiratory movements; it is conditioned by the general increase of muscular tonus, affecting primarily the expiratory muscles, whilst expiration is obstructed by closure of the glottis. The result is an increase in the intrathoracic pressure. On two occasions I have connected a manometer with the needle in cases in which paracentesis of the thorax was being performed for pleural effusion. In each case any voluntary effort on the part of the patient was accompanied by a well-marked rise of the intrathoracic pressure. The expiratory and inspiratory oscillations were markedly decreased. Turning to the effect of effort on the intracranial pressure we see what are the results of these respiratory changes. In the spring of 1914, together with W. L. Symes, I made some observations on the alterations of pressure of the cerebro-spinal fluid on a number of cases of cerebral syphilis who were being treated by the then fashionable remedy of injection of salvarsanised serum. Hitherto all observations of the intracranial pressure have been made with patients who have been trephined, and the pulsating skin and membranes over the trephined area have had their excursions directly recorded by a tambour. The advantages of the estimation of the pressure of the cerebro-spinal fluid by lumbar puncture in the intact organism over this method are sufficiently obvious, and its delicacy is very much greater. We examined in all six cases and found that the cerebro-spinal pressure responds to the slightest physical or intellectual effort by a marked rise. Our observations showed moreover the great influence of respiration on the cerebro-spinal pressure. Fig. 14 shows well the enormous fluctuations that occur with deep inspirations and expirations and the huge rise when the breath is held. The increase of the intrathoracic pressure during effort is the chief if not the only cause of the concomitant rise of intracranial pressure.

EFFORT AND CIRCULATORY REACTION.

Since the fundamental work of Mosso the response of the circulatory system to cerebral activity has been the subject of a great deal of investigation. The increased frequency of the heart to intellectual effort is well shown in the slide. It is of some interest to discover whether this increased frequency is determined by accelerator stimulation or by removal of the vagal control. For this purpose I took some records with a much faster rate of movement of the photographic paper than in the record shown, and measured the time relations of the systole and diastole.

FIG. 14.



Simultaneous records of the cerebro-spinal pressure (upper line) and the respiration (lower line). Between 1 and 2 breath was held, 3 and 4 are deep inspirations.

Reid Hunt found that by stimulating the accelerator nerve the times of systole and diastole are decreased together, while with a loss of vagal control the loss of time is confined to the systole. My records all show that the systolic time is unaffected, whereas the diastolic time is diminished; thus the effort is responded to by a diminution of vagal tonus. The blood pressure is again very generally known to be increased in effort, and we shall see that in certain types of neurasthenia this increase is either very small or absent. The criticisms of Pachon have shown that the method commonly practised in this country of taking the records of the pulse at the wrist while the artery is compressed higher up is unsound; this is particularly true when investigating the changes accompanying effort and affective states in which there is reason to believe that vasomotor changes at the extremity of the limb are most marked. On the other hand, to record the pulse at the site of the application of pressure, that is, from the pulsations communicated to the Riva Rocci bag, precludes the use of tambours whose sensitiveness is affected by variations in internal pressure. For this reason I have connected the bag with a mercury manometer and photographed the pulsations (Fig. 15). It will be noted that contrary to the observations of Schrumph and Zabel the systolic and diastolic pressures are both increased. It does not appear to me to be possible to apportion the relative degrees of influence exerted by the heart and the vasomotor system in this reaction.

The vasomotor changes in the peripheral circulation in response to cerebral activity have been much studied, and the observations of Lehman and Weber—to mention only two of the writers who have most concerned themselves with plethysmographic studies

FIG. 15.



Photograph of pulse oscillations of mercury column at different pressures of Riva-Rocci bag A when subject is at rest, B during calculation. The arrows point to beginning of pulsations and to the maximum oscillation.

—agree in recording a fall in the volume of the limb as a sign of effort. The vaso-constriction continues throughout the period of effort, and should the effort have been sufficiently intense to cause discomfort

its cessation is followed by an increase in the limb volume to a greater size than before the beginning of the effort. We shall consider this after-effect when we study the objective signs of affective states. Weber has recorded alterations in the intra-abdominal pressure accompanying cerebral activity which he ascribes to a variation in the blood-supply to the intra-abdominal viscera.

EFFORT AND VISCERAL REACTION.

What we have seen of the increased muscular tonus during effort and the respiratory variations makes any interpretation of results obtained by introducing balloons into the hollow viscera exceedingly difficult. That many important visceral changes accompany cerebral activity is, of course, certain, in fact, they constitute the most important part of the bodily accompaniments of such activity, but so far their investigation has to be conducted by methods adapted to show chemical rather than gross motor variations. Lange has described fluctuations of the "active sense attention"—*sinnliche Aufmerksamkeit*—the existence of which is shown by the fluctuating appearance and non-appearance in consciousness of a minimal sense impression. I have objectively demonstrated fluctuations of effort; for this purpose the subject was instructed to hold a wand in his hand and to keep the point of it in the middle of a small ring, suspended from a stand. The ring was lined on the inside with a hollow thin-walled rubber bag, which was blown up to a low degree of tension and connected at its orifice with a recording tambour. The quadriceps tonus and the respirations of the subject were recorded on a drum together with the pressure in the bag. A slight movement on the part of the subject would lead to the wand touching the bag and the increment of pressure was recorded by a movement of the tambour lever. When the touches on the ring bag were most frequent there was a diminution of the quadriceps tonus and an increase in the depth of the respirations. The back of the subject was turned to the drum so that he could not observe what was taking place. In this fashion it was possible to demonstrate fluctuations of the effort coinciding with periods of inaccuracy in the handling of the wand. Such periods became more frequent as the subject became fatigued, and in certain cases of neurosis complaining of nervous asthenia they were particularly frequent.

I have so far endeavoured to give some brief account of the movements that are the objective expression of effort. The first portion of my next lecture will be devoted to the consideration of the relationship of such movements to the sensory phenomena that are the concomitants of mental and physical effort.

LECTURE II.

IN the preceding lecture we reviewed some of the objective aspects of effort. Before proceeding to study the other bodily concomitants of cerebral activity, I wish to summarise what objective study has taught us of the state of activity that we designate as effort. In the first place, all the phenomena recorded were in the nature of increased bodily activity and not of the inhibition of activity, that it might be thought would permit the more readily the uninterrupted response of the specific mechanism to the stimulus. We found that the generalised bodily reaction of effort bore a direct relation to the difficulty—that is, to the chance of failure of the specific mechanism in performing its appropriate action and we noted that when this bodily response experienced any diminution, the accuracy of the specific performance was likewise diminished. Lastly, we found that the net result of such of the bodily changes observed in effort was to increase the general efficiency of the body, whether by accelerating and increasing the simpler motor reflexes or by influencing the blood-supply of the nervous system by an increase of the intrathoracic pressure and vasomotor changes.

Now let us interrogate our consciousness as to the feeling that we experience during effort. As in the case of other affective states that we shall study later, we find that to attend to a feeling is, to a great extent, to lose it. We are aware of certain respiratory sensations, a certain sense of increased cardiac action, of intracranial pressure, and of postural tension. Sometimes one, sometimes another of the constituents of this feeling of effort becomes so dominant that the vague feeling is swamped by a distinct sensation such as I instanced in the case of the respiratory symptoms experienced in performing a count of the particles ingested by phagocytes. The general sum-total of the sensory presentation of the bodily changes of effort is a disagreeable one. The sooner that we can cease from effort and find our specific task performed the better pleased we are.

Ribot has emphasised the fact that nobody really has pleasure in work itself, it is to its accomplishment that we really look forward with pleasure. Now whether we regard effort from a purely mechanical point of view, or whether we take cognisance of its affective aspect, the conclusions that will be drawn are much the same. A stimulus is presented, the specific response to which is inadequate, or else the task would be accomplished with mathematical certainty. When such a stimulus fails to arouse an adequate response on account of its own feeble nature, nothing further happens except that the response will itself be a feeble one. When, however, the stimulus is powerful and insistent and the mechanism of response is inadequate another and more diffuse constellation of reflexes is aroused. Various bodily activities are brought into action, all of which tend

to increase the efficiency of the specific mechanism. The sensory presentation of these bodily activities is a disagreeable feeling which we do our best to allay by accomplishing the specific action demanded. Viewed from this angle we shall see that the mechanism of effort resembles that of the affective states that we are about to consider, and further, that no distinction can be drawn between effort and the conception of attention as propounded by Locke and in a less incisive fashion by Hamilton. It will be obvious that when through either innate or acquired disability the specific mechanisms are everywhere inadequate to respond to the tasks that they are called upon to perform, the never-ceasing activity of the mechanism of effort will prove exhausting to the body, and in its sensory aspects a most distressing form of neurotic disturbance.

REACTION MANIFESTED BY CHANGE IN ELECTRICAL PROPERTIES OF THE SKIN.

Hitherto the reactions that we have studied have been occasioned by the activity of striated or non-striated muscular tissue. I now propose to deal with a reaction that is manifested by change in the electrical properties of the skin. This reaction was first described by Féré in 1888 as an emotional response, manifesting itself by a diminution of the resistance of the body to the passage of an electric current. Galvanometric deflections occurring when the skin was explored by a pair of electrodes were independently described by Tarchanow in 1890, and found by him to occur as responses to physical and psychical stimulation. He considered them to be due to secretory currents of the skin glands.

The investigations of both of these observers were to a great extent ignored, and the same fate befell Stricker's confirmation of Tarchanow's experiments in 1902. It was not till 1904 that the subject was reinvestigated, when Veraguth, stimulated by some preliminary observations on bodily resistance by E. K. Müller, confirmed the observations of Féré and gave the first systematic exposition of what he termed the "physico-psycho-galvanic reflex." He described this reflex as a diminution of the resistance of the skin to the passage of a constant current occurring as a response to stimuli which caused an alteration of the affective state. It is not possible in the course of these lectures to deal with the mass of observations that have since accumulated from the work of the many experimenters who, subsequently to Féré and Veraguth, have investigated this phenomenon. Nor are we concerned for the moment with the physical nature of the response. It is sufficient to state that the galvanometric effect is beyond all doubt due to a diminution of the electrical resistance offered to the passage of a constant current by the skin, and that this diminution is exhibited as a maximum effect in the palms of the hands, a little less obviously in the sole of the foot, and scarcely at all in other parts of the skin. This statement, which is founded on the careful exploration of all parts of the body surface

by Gildermeister, has been confirmed by every observer who has worked on the subject.

The work of Crile and his pupils has shown that an increase of electrical conductivity, or conversely a diminution of resistance, is associated in all tissues, with an increase of their metabolic activity; we may tentatively regard the galvanic response as a sign of the increased activity of the gland-bearing area of the skin. If it be to the activity of the cutaneous glands themselves that we must ascribe the galvanic reflex it is certainly not due to the gross manifestations of that activity by the excretion of sweat. In 1918 I had a neurotic patient who suffered from hyperidrosis of both hands, the sweat falling off from the tips of the fingers in drops. I found that this patient exhibited the galvanic response to all adequate stimuli in a marked degree, although the palms were covered by a thin layer of sweat, and it was unthinkable that any actual increase in the amount of fluid excreted should have an influence on the conductivity of the sodden skin. I showed the case to Prof. Waller, and he also remarked on the magnitude of the galvanic response given by this patient. It is further obvious that the galvanic response, if it be associated with glandular activity, can only be governed by the centrifugal nerve impulses that travel through the fibres of the sympathetic, and we shall later see reason to believe that, in common with all the other mechanisms which take part in the general bodily reaction to noxious stimuli, the galvanic reaction is conditioned by the response of the thalamic system. That changes in the peripheral blood-supply have nothing to do with the response was shown by the experiment of Veraguth, who obtained normal responses from a limb exsanguinated by an Esmarch bandage.

I now propose to deal with some of the aspects of the galvanic reflex that will prove of service in the objective study of the bodily response to cerebral activity. Before doing so, I will indicate briefly the technique that can be usefully employed for this purpose. In my own experiments I have been in the habit of measuring the bodily resistance to a current of a couple of Leclanché cells which is passed through the body from two liquid electrodes of normal saline into which zinc terminals dip. The subject is seated with the hands immersed one in either electrode, and forms the fourth arm of the familiar Wheatstone bridge circuit. I prefer the liquid electrodes to the solid zinc electrodes strapped on to the back and front of a single hand, because slight shifting of the electrodes due to movements occurs rather easily when the latter procedure is adopted; further, the low resistance measured allows its easy demonstration to the uninitiated without having to multiply up the results by using unequal ratio arms in the resistance box. The point is, of course, of no importance. For experimental work I have abandoned the moving coil galvanometer for the Einthoven instrument, since with this type of galvanometer it is alone possible to measure time relations with any degree of accuracy, and an additional interest is given to the records by

the appearance of the heart beats in the curves. Further, with the double-string instrument which I owe to the generosity of Mr. Alfred Teniers it is possible to obtain either simultaneous records of the galvanic response of two parts of the body or of muscular or respiratory variations accompanying the galvanic reflex.

NATURE OF STIMULUS EVOKING GALVANIC RESPONSE.

The first subject for inquiry is as to the nature of the stimulus that evokes the galvanic response. Practically all those who have concerned themselves with this reflex agree that stimuli adequate for the galvanic reflex are capable of causing an affective state. We are in no way entitled to draw the inference that the occurrence of an affective state is necessary to the exhibition of the reflex, and still less that the occurrence of the reflex conditions an affective state. While the examination of the relation between bodily activity and states of feeling may be reserved at this stage for later discussion, it must here be pointed out that an affective state, to exist at all, must be experienced by the subject. Now, a galvanic response may occur without the subjective experience of an affective state. I have frequently observed a response to be elicited by a stimulus when the subject affirms that the stimulus has for him no feeling tone. This may be best observed in the performance of word association experiments. The response to a certain word may be marked and yet when the subject is interrogated he is at first unable to discover any association of emotional significance in the word, and, moreover, he assures me that the word left him absolutely indifferent. It is true that further examination generally succeeds in recalling a hidden emotional significance, and thus reveals that the stimulus activated a specific reflex system that at one time had a nexus with the mechanism of feeling; but that is not the point. If we accept the assurance of the subject, we must believe that the reflex occurred without his experiencing any feeling connected with the word. To talk of a subconscious feeling is, of course, to talk nonsense. The same point may be verified by purely introspective investigation. When a painful or presumably painful stimulus is applied to the hand, such as touching it for a moment with a flaming match, a well-marked reaction will be obtained.

If, however, the experiment be repeated a number of times in succession without the injury inflicted corresponding to that which was anticipated at the first stimulation, the subject becomes indifferent and possibly bored with the performance, and yet with each application of the stimulus there is still a galvanic reaction though the subject is well assured that he feels no apprehension. To appreciate the cogency of the experiment one must oneself serve as a subject, and there is no mistaking the genuine surprise with which one observes a reaction to a stimulus that has become a matter of indifference. I shall refer to this experiment again when we come to discuss conditioned reflexes. Here its importance lies in the

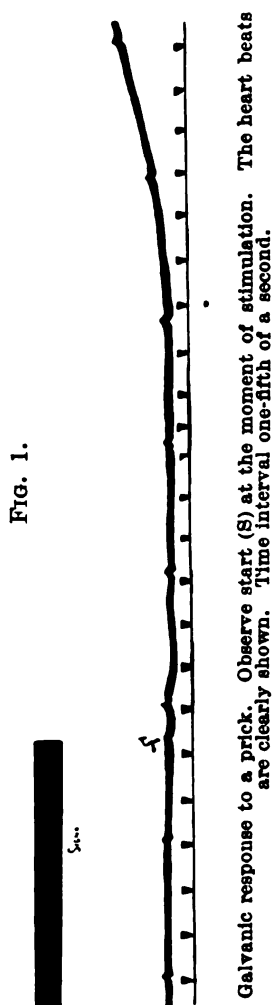
fact that the reaction takes place in the absence of an affective state. Many observers have maintained that the galvanic reflex accompanies mental effort as well as states of feeling. We have just now discussed the sensory concomitants of effort and I hope to have succeeded in demonstrating that they constitute what we know as an affective state; but I do not consider that they are normally accompanied by a galvanic reaction. When, however, an intense effort results in one or other of its sensory factors assuming overwhelming proportions, we have said that it is presented as a distinct disagreeable sensation and may as such arouse the same system of reflexes as it would were it a sensation caused by a specific stimulus. In this connexion I instanced the feeling of suffocation during a cell count. In the performance of word association tests I have generally found that the first three or four word reactions in the examination of a new and nervous subject are accompanied by a galvanometric deflection, even though they be essentially neutral words. This is simply an expression of the state of anxiety on the part of the subject, who soon settles down and responds electrically only to words having an emotional significance.

PARTIAL CLEARING UP OF CONFUSION BETWEEN SUBJECTIVE AND OBJECTIVE STANDARDS.

These considerations indicate some of the difficulties to be encountered in any attempt to elucidate the meaning of a physical response by an appeal to subjective evidence; a similar confusion of subjective with objective standards has proved to be such a stumbling-block in the physiology of the afferent nervous system. In that case the problem for the physiologist is not what is the presentation to consciousness following on the stimulation of an afferent nerve-ending, but what are the reflexes that such stimulation evokes, and by what form of stimulus is the receptor organ excited. Thanks to the introduction of the idea of the existence of a system for the transmission of nocuous stimuli by Sherrington, and its correlation with the thalamic reflex system by Head and Holmes, the physiology of the nociceptoral nervous system has been made relatively clear, and we have eliminated many of the obscurities that were so perplexing when the subjective sensations of the patient were our only guide. Likewise, in considering the galvanic reflex the first question to be considered is what are the objective characteristics of the stimuli that evoke this increase of conductivity on the part of the skin—an increase which we have reason to consider to be an index of a general increase of functional activity and to be correlated to certain states of feeling. The answer is that in the first place any type of stimulus that tends to cause damage to the body, or that threatens such a change in the environment as is likely to result in bodily damage, will prove to be an adequate stimulus. In the second place we must recognise not only actual bodily damage but the disturbance of the smooth working of bodily activities as the characteristic of another class of stimuli which will evoke the generalised

bodily reaction of which the galvanic reflex is a sign. The first class of these stimuli is represented by such physical disturbances as may result from a blow, a burn, a prick or pinch; or those acting from a distance, such as loud sounds, blinding lights, or noxious smells; or, again, endogenous stimuli, such as colic or neuralgia.

Fig. 1 shows a typical reaction as registered by the string galvanometer to a prick, the initial muscular

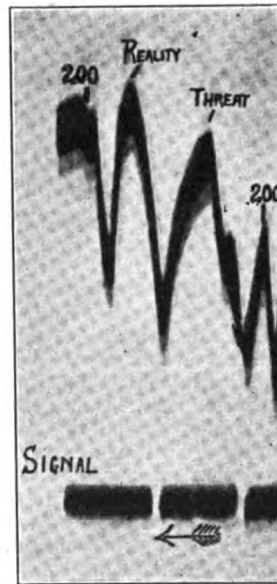


start of which we shall have more to say is clearly seen. If now we proceed to use verbal stimuli instead of actual physical procedures we are using a type of stimulus belonging to the second category of our classification. The simplest form of verbal stimulus will be the threat of the application of a noxious physical stimulus. Fig. 2 shows the responses to the threat of a prick and to an actual prick. Here

we might hope to obtain some light on the relations of the two nervous mechanisms aroused. In this particular case you will note that the response is as great to the threat as it is to the act. I should like to be able to say that it was possible to correlate the mentality of my subjects with the relative efficiency of the two stimuli, but the results obtained from a large number of observations have been too inconstant. There are probably too many factors involved in the experiment—the degree of dramatic conviction with which the threat is performed, the attention of the patient, and the relative severity of the actual physical stimulus, must all be variables.

The threat to cause bodily discomfort is the simplest form of verbal stimulus. From this point onwards the stimuli may be elaborated by the representation of circumstances either past or present that are opposed to the well-being of the subject or are in conflict with the general tendency of his conduct—that is, stimuli such as will on the affective side evoke the feelings of grief or anger. So much for the galvanic response to external stimuli, but even more important is the galvanic response to stimuli whose immediate origin is in the autogenous neural processes of the subject. The spontaneous representation of some disagreeable or painful circumstance will serve equally well to elicit the galvanic reflex. Whether the subject recalls silently some past experience of a painful nature or whether he communicates it verbally to the observer the representation will in both cases evoke a diminution of skin resistance. We can now determine objectively the nature of the stimuli that will evoke the reflex without any further appeal to the evidence furnished by subjective inquiry. We note that one and all the stimuli have this property in common—their continuance is inimical to the well-being of the subject. Obvious as this is for the physical stimuli, it is no less clear when we consider the stimuli derived from outside verbal suggestion or from the representations evolved by the subject's own activities. The representation of an old pain must, if it be sufficiently vivid, involve all those reactions that occurred with the original stimulus. In so far as it falls short of representing them it falls short of being a vivid impression. I need hardly remind you

FIG. 2.



Galvanic response to burn and threat of burn. Graduations of diminution of resistance by 200 ohms.

that a representation must call into activity those nervous mechanisms that were aroused in the first instance, and that their necessary modification by subsequent neural associations constitutes the difference between the actual and the revived experience. In so far as the bodily response is concerned, the stimulus will in both cases be of the same nature as the initial physical stimulus, and from the objective point of view the reflex increase of conductivity evidences the same type of nervous activity. Fortunately for ourselves the representation can never or very seldom occur in anything approaching its first intensity. In many instances it cannot recur at all in a normally constituted organism.

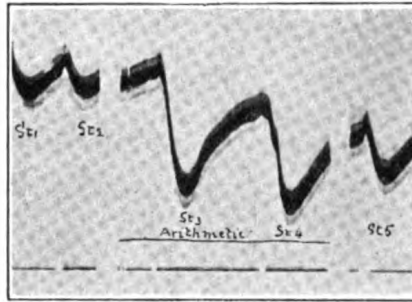
THE GALVANIC REFLEX NOT UNDER VOLUNTARY CONTROL.

The completeness of representation is the test of the degree in which the activities of the organism as a whole have been modified by the original experience. I try to recall an old toothache and I succeed in recalling concomitant experiences, but not a twinge of the original toothache. I recall a profound grief, and I shall feel much of my pristine pain and sorrow. Now the galvanic reflex distinguishes between these two types of representation, and this is what makes it so valuable for the objective study of cerebral activity; in our inner lives we are not always quite sure ourselves as to whether we have really any feeling about a subject—that is, whether it evokes a bodily resonance or whether it is merely a subject about which we think that we ought to feel strongly, whereas, in fact, it fails to arouse any bodily response. It is the objective demonstration of these two states that is furnished by the galvanometer. Anyone who cares to sit quietly by himself and recall past experiences whilst connected with the galvanometer circuit will learn much about matters that he has hitherto taken for granted. The resistance reaction is not under voluntary control; it is impossible to evoke it by simulation of affective states, such as a fictitious rage, nor can the mere recitation of emotional poetry, no matter with what emphasis it be declaimed, produce a reaction unless by some chance a phrase acts as a stimulus to evoke some association with a personal experience of affective import.

I will now pass on to consider some of the other aspects of this reflex that are of importance in affording information as to the relations of the mechanism of bodily reaction accompanying affective states to other nervous mechanisms. The reflex cannot be inhibited by any voluntary effort on the part of the subject. I have sought for evidence of inhibition either of the response to physical or verbal stimuli in over a hundred subjects, but have never met with evidence of any direct voluntary power to either inhibit or modify the reflex. When the stimulus is not a maximal one the response may be modified to some extent by the activities of the subject at the time of stimulation. Fig. 3 shows the response to a moderately loud auditory stimulus, first, when the subject was expecting the stimulus; next, when he

was engaged in mental arithmetic ; and lastly (Fig. 4), when he was subjecting himself to a very painful faradisation applied to the sole of the foot. When I first obtained this result it seemed strange to me that the response to an irrelevant stimulus should be greater during the performance of arduous work than

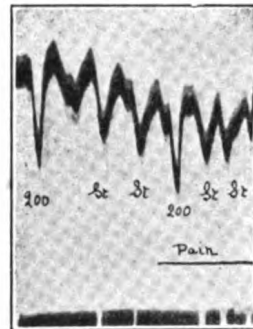
FIG. 3.



Reaction to uniform stimuli (prick).
1 and 2 before, 3 and 4 during, and 5
after mental arithmetic.

when the nervous system was keyed up to expect the stimulus. The work performed, be it noted, was not responsible for any diminution of resistance per se. I have, however, constantly obtained this modification of the reaction to moderate stimuli, slight though it be, so long as the work on which the subject is engaged does not prove unduly irksome. When the resentment or the discomfort of strenuous work

FIG. 4.

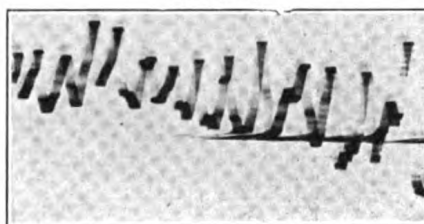


Reaction to uniform stimuli
(prick) before and during
painful faradisation.
Graduation of 200 ohms.

reaches such a pitch as in itself to produce a bodily reaction in the shape of a diminution of resistance, the response to the initial stimulus is diminished, just as we see occurred in this record when the subject was undergoing painful stimulation. When, however, the stimulus is a maximal one, such as is produced

by the firing of a pistol close behind the subject, it ceases to be possible to modify the response either by work or by any moderate degree of pain. Fig. 5 is the record of what is apparently a fatigue effect in the galvanic response to a series of uniform auditory stimuli. This apparent fatigue cannot be attributed to exhaustion of the effector mechanism of the response, that is either to the skin, the centrifugal nerves going thereto, or the nerve cells governing them, for if an adequate stimulus of a different nature to that of the series be administered at the beginning and at the end of the series it will be found to evoke approximately the same degree of response. Under the conditions of the experiment, which consists in

FIG. 5.



Fatigue effect of galvanic reflex to uniform series of sound stimuli.

the production of a short series of sounds of equal and moderate intensity, the effect cannot be due to fatigue either of the peripheral receptor mechanism or of the cortical receptor centres. We may therefore ascribe the progressive diminution of the response to some change occurring in the nervous mechanism connecting the receptor system with the effector system of the galvanic reflex. The term "progressive indifference" probably describes this change better than fatigue; for if in the middle of the series of moderate stimuli we intercalate one of greater magnitude we obtain a response approximately equal to that aroused by a stimulus of the same magnitude administered before the beginning of the series. It is noteworthy that after the intercalation of the powerful stimulus the descending series of responses is interrupted for the next two stimuli which show some degree of augmentation.

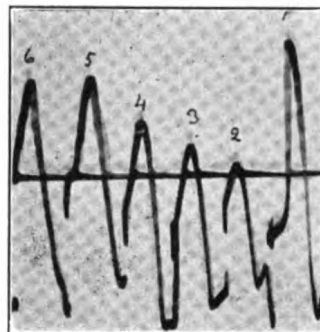
VARIATION OF RESPONSE WITH STIMULUS.

When the patient is subjected to a brief examination not lasting over ten minutes or so the magnitude of the response can be shown to vary directly with the strength of the stimulus. Fig. 6 shows the response to a series of break induction shots of increasing strength. This relation between the strength of the stimulus and the response is obviously a fact of some importance, but we must hesitate before we pronounce on the relative efficiency of any two verbal stimuli or stimuli evoked by the subject's own representations on the strength of an examination of the galvanic responses elicited. Even with simple and easily controlled physical stimuli two such stimulations of

different strengths can only be counted upon to give proportionate responses when they are not separated at too great an interval and the general attitude and condition of the subject is approximately the same. After an initial intense stimulus with its concomitant response the resistance does not immediately rise to the old level, and so long as the slight general diminution in resistance continues the response to subsequent stimuli, of whatever their nature, will be somewhat greater than formerly. In the study of the galvanic reactions of neurotics undergoing a prolonged examination this tendency must not be overlooked.

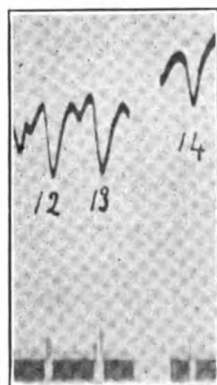
If a painful stimulus be repeatedly administered, and its administration be accompanied by some sound or movement on the part of the observer, after a time the repetition of this sound or movement will be in

FIG. 6.



Response to series of break induction shocks. 2 coil at 10; 3 coil at 8; 4 coil at 6; 5 coil at 4; 6 coil at 2; 1 graduation 400 ohms. Final graduation omitted.

FIG. 7.



A conditioned reflex.—Upper line, the galvanometer, lower broad line the signal response. 12 and 13 are the last in a series of painful stimuli. For 14 the stimulus is short-circuited, but patient still responds on hearing the click of the key.

the painful stimulus, which was an induction shock, was administered, the subject who sat with his eyes closed heard the click of the key that opened the

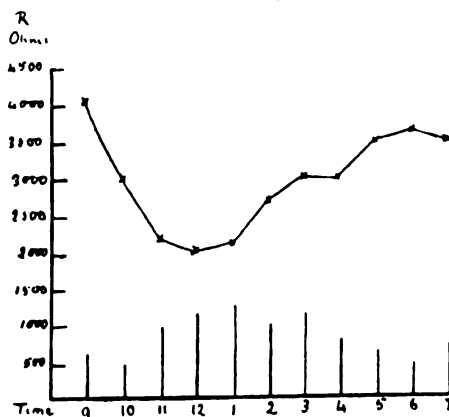
itself sufficient to produce a response equal to that caused by the stimulus. We shall, in fact, have established what Bechterew calls a conditioned reflex. Fig. 7 shows such a conditioned reflex. A painful stimulus was administered to a subject who was instructed to press a key which completed the circuit of an electric signal every time that he felt the stimulus. In addition to the motor reaction the galvanic reaction to the stimulus was recorded. Every time that

circuit for the break induction shock. After the reaction had been repeated a sufficient number of times the key was clicked as usual, but the current was prevented from reaching the subject by a previous disconnexion of the circuit. On hearing the accustomed click the subject reacted in the accustomed fashion both by the signal and by a galvanic response, which will be seen to have been of no less magnitude than that responding to the last two occasions of the series when the induction shock was really administered. We shall see in the next lecture what light a consideration of these conditioned reflexes throws on the relation between the bodily response and the affective state.

PROBLEM OF SKIN RESISTANCE.

The relation of the initial resistance of the skin to the magnitude of the galvanic response is a very difficult point to determine. Waller has shown that the skin resistance undergoes a diurnal variation following closely the diurnal variation of temperature. I took advantage of this observation to determine the relation of the galvanic responses evoked by

FIG. 8.



Graph showing rough correspondence through the day between skin resistance and galvanic reflex.

uniform stimuli to the initial skin resistance. Maximal stimuli were used, and for this purpose I found a pistol shot most convenient. A rough correspondence between the resistance of the skin and the galvanic reflex throughout the day is shown by Fig. 8. This chart represents the mean of observations conducted on three successive days, but the difficulties in obtaining the subject at any one time under approximately the same conditions are very great. For what it is worth, it seems to indicate clearly that the maximum response occurs round about mid-day when the

resistance of the skin is at its lowest. How far we are justified in assuming that cerebral activity is at its maximum at this time is very doubtful. Most people have the impression that their work is better performed either in the early morning or late at night, but this opinion is perhaps of little value. We judge of our work after all by much the same standards as those by which the world at large assesses our personal value. Everyone knows that the chief conditions of worldly success are great industry combined with a fair amount of stupidity, or—to put it less bluntly—with an absence of that self-criticism that so often destroys the power to accomplish things by leading us to inquire as to whether they are really worth doing. Similarly, the greater facility with which work is conducted at hours remote from the mid-day interval may simply be an expression of the abeyance of similar critical and inhibitory processes.

I have been unable, in spite of the large amount of material investigated, to secure any data as to a correlation between intelligence and the galvanic response that would appear to be sufficiently trustworthy to justify its inclusion in this review. In this connexion the work of Miss Waller appears to be highly important. She examined the galvanic responses of a class of 70 students to a series of standardised stimuli. The students shortly afterwards underwent an examination in physics. Correlating the marks obtained and the magnitude of the galvanic responses Miss Waller found that the average response of the higher placed half of the class in the results of the examination was greater than that of the lower half of the class. A further investigation on these lines is at present urgently needed.

IMPORTANCE OF LATENT REACTION TIME.

The latent time that occurs between the stimulus and the galvanic response is, as we shall see later, a matter of great importance in the elucidation of the significance of the bodily reactions. I have a large number of records, taken with the Einthoven galvanometer, which show the latent period in response to a variety of stimuli. To a physical stimulus, such as sound, the reaction time may be as long as 2·5 seconds, when the stimulus is a single loud tap on the table, whereas it may be as short as 0·8 second to a pistol shot; the latter figure was given by a young man with very large galvanic responses who was suffering from diabetes, a condition which we are accustomed to associate with hyper-excitability of the sympathetic system. The duration of the response is, in the case of a physical stimulus, conditioned primarily by its initial magnitude. As we have already noted, a response of great magnitude may be followed by an after-effect lasting for a considerable period, often three or four minutes. When we are dealing with verbal stimuli the latent period may be very long, the association processes necessary to evoke the response may be complex, and the duration of the response may be greatly lengthened owing to perseveration.

SPECIFICITY OF THE GALVANIC REFLEX TO NOCUOUS STIMULI.

I have now dealt with some of the main facts that have so far presented themselves from the study of the galvanic reflex, and I have especially dwelt on the nature of the stimuli that evoke this reflex. We have seen that to divide them into physical and psychical stimuli is from the objective point of view unjustifiable, since all these forms of stimulus have in common the property of injuring or inhibiting the normal course of vital activity. In future, in speaking of such stimuli, it will be convenient to assign to them collectively the same name that Sherrington has bestowed on those belonging to the physical class, and to refer to them as nocuous stimuli. The galvanic response is not the only type of response to nocuous stimuli that we know of. We have seen that it is an inevitable response incapable of any great degree of modification by other forms of activity, but this characteristic it shares with a number of other responses that we may study objectively. It has, however, one characteristic that at once makes its study of paramount importance in any objective investigation of neurosis, and that is that, alone of all the forms of bodily response that we shall study, it is specific to nocuous stimuli. It does not primarily occur as a bodily sign of the state of cerebral activity that we have considered already as effort.

OTHER OBJECTIVE SIGNS OF RESPONSE TO NOCUOUS STIMULI.

Now, in investigating further objective signs of the response to nocuous stimuli we shall find that we have met with all these signs in the study of effort. The diffuse increase of muscular tonus that we have already seen to be manifested both by movements of the extremities and by induration of the muscle occurs also as a response to nocuous stimuli of sufficient intensity. Fig. 9 shows a record of the movement of the foot caused by increased tonus of the

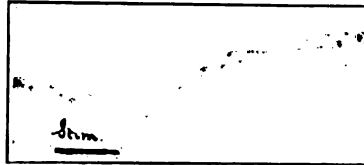
FIG. 9.



quadriceps as a response to a painful stimulus. Fig. 10 is the photographic record of the increase in tonus of the arm muscles to a nocuous physical stimulus recorded by the optical lever. The movements of the head recorded by the method described in the previous lecture are, however, of a nature different from that of those elicited by effort. You may remember that the tonic response to effort was manifested by a forward movement of the head.

A painful stimulus is responded to by a retraction of the head. This might appear to be an example of a purposive movement, the subject endeavouring to withdraw from the vicinity of the painful stimulus. but on applying the stimulus to the back instead of in front the same retraction of the head occurs, though in this case the subject is moving in the direction of the stimulus. It cannot, therefore, be

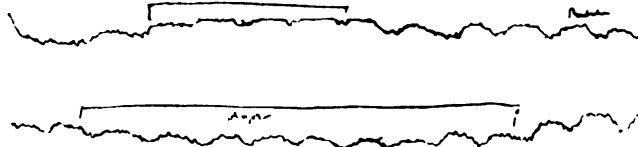
FIG. 10.



Photographic record of the increase in tonus of the arm muscles to a nocuous physical stimulus, recorded by the optical lever.

compared to the type of reflex that occurs when a spinal animal withdraws the foot from a nocuous stimulus. Disagreeable and offensive verbal stimuli will also elicit this retraction reflex (Fig. 11), which—in contradistinction to the forward movement accompanying effort—appears, therefore, to have some of the specificity to nocuous stimuli that characterises the galvanic reflex. The respiratory

FIG. 11.



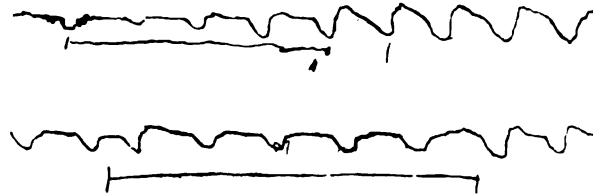
Opposite movements of head. Forward with effort (recitation). Backward in response to offensive (verbal) stimulus. Respiratory and circulatory movements shown.

changes do not differ, so far as I have been able to observe them, from those associated with effort. Fig. 12 is the record of two interesting tracings obtained, one as the reaction to a painful thought and the other to anger. The response in both cases is manifested as a flattening of the respiratory curve that we have seen reason to associate with increased muscular tonus. I am aware that many observers have attempted to demonstrate the existence of special forms of the respiratory curve associated with specific affective states, but the lack of uniformity in their results, which depend on measurement of the expiratory and inspiratory excursions, have failed to convince me that they are dealing with any specific reflex changes. The heart rhythm is accelerated in

response to nocuous stimuli, but such acceleration, when it occurs, is of very short duration in response to a short-lived stimulus. With prolonged stimulation the cardiac rhythm is accelerated for the whole duration of the stimulus. Again, if the inferences drawn from measurement of the time relations of the cardiac cycle are to be trusted, it appears that the acceleration is due to depression of the vagal inhibitory and not to stimulation of the accelerator mechanism.

The evidence furnished by plethysmographic tracings of the vaso-motor reactions occurring in the limbs must be accepted with a certain amount of reserve. In the well-known Mosso plethysmograph as modified by Lehmann there are two possible sources of error which it is practically impossible to eliminate. First, a very small amount of displacement of the arm will cause a very marked effect on the plethysmographic curve and will be interpreted as an increase of volume if the arm be moved forward and as a decrease of volume if the arm be withdrawn

FIG. 12.

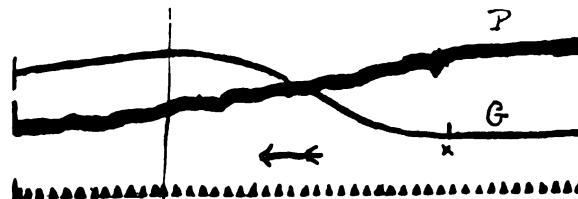


Respiratory tracings. The upper tracing shows effect of anger. The lower that of grief. The period during which the subject was indulging in the thought of the vexations and the painful experiences is indicated by the straight line below the tracing. (To be read from right to left.)

ever so slightly from the plethysmograph. That such slight movements do occur and cannot be consciously guarded against is shown by the old experiments with an apparatus known as the "automatograph." In these experiments the partially flexed forearm is suspended in a cradle hung from a support. The movements of the cradle are recorded on an underlying drum and it is claimed that by this method it is possible to show that a disagreeable stimulus is responded to by retraction of the arm and an agreeable stimulus by its advancement. I have not adopted this method in my investigations, because I consider that it harbours many fallacies; but whatever the interpretation we may place on them, results thus obtained show that such movements certainly do occur. Another source of fallacy in the use of the plethysmograph becomes obvious from the evidence that I have submitted as to the diffuse increase in muscular tonus occurring as a bodily reaction in certain states of cerebral activity. Such an increase in muscular tonus must occasion an alteration of muscle volume simulating a vaso-constriction. I have dwelt on the shortcomings of the plethysmograph because we shall see later that results obtained

from this instrument are the chief support for the assumption of a bodily response occurring in exactly the opposite direction to that elicited by nocuous stimuli. In order to avoid one source of error—that arising from slight movements of withdrawal or propulsion of the limb—I have designed a form of plethysmograph that has yielded fairly satisfactory results in these experiments. It is in essence a light metal drum covered at either end by a stout rubber diaphragm. There is a circular hole in each diaphragm, large enough to allow the passage of the arm whilst permitting a firm gripping of the limb by the thick rubber. The arm is thrust through both diaphragms so that the hand and wrist project beyond the further one, whilst the proximal end is a couple of inches below the elbow-joint. The drum is connected to a type of Brodie bellows recorder in which the bellows is replaced by a thin rubber “condom.” The plethysmograph hangs freely on the arm, which is supported by two blocks at the wrist and elbow. Using an instrument of this type, which cannot be affected by any slight movements of the arm, in the direction of withdrawal or propulsion, I have obtained records of diminution of limb volume that are in accordance with those obtained by previous observers. It will be noted, however, that this arrangement of the plethysmograph cannot altogether neutralise, though it sensibly reduced, the error that arises from changes in muscle volume as a result of increase of tonus. The only method of plethysmographic recording that would be free from both these errors is that adopted by Weber who used an ear plethysmograph. I confess that the extremely disagreeable features of this method, which involves the working of large amounts of vaseline into the

FIG. 13.



Simultaneous record of galvanic (G) and plethysmographic (P) responses to a prick, x.

hair, have prevented me from proposing its use to the subjects of my experiments. Fig. 13 shows a photographic record of the plethysmographic and the galvanometric responses to a nocuous stimulus. It will be observed that the latent period is identical in the two forms of response.

RESPONSES TO BENIGN STIMULI.

Now so far we have considered the bodily response to nocuous stimuli, that as to stimuli that tend to disturb and destroy life, and we have, moreover, noted that the sensory concomitant of such responses

has been a feeling of an unpleasant nature. We may now fairly envisage the question as to what are the responses to stimuli that tend to further and perfect life—what we will call benign stimuli—which so far as they have any sensory reaction affect us pleasantly. Since the galvanic reflex is the only response that we have so far been able to study that is specific to nocuous stimuli and is not elicited by effort, it is to this reflex that I shall first turn for an answer. I have found that to stimuli of a benign nature there is either no response at all or else a slow increase in resistance occurs; but this slow alteration of resistance is only to be noted when the preceding state is one of the low resistance that we consider to be indicative of general bodily activity. If, after a series of painful or vexatious stimuli the attention of the subject be diverted to more pleasurable matters, the lowered resistance rises gradually until a point above the initial neutral state has been reached. If a hungry subject be given a satisfying drink and appetising food the resistance will show a slow increase. If a subject who has taken up his position, rather dreading a series of irksome experiments with painful electrical shocks, be told that for that séance the observer only purposes to take some simple pulse records this welcome news is followed by a slowly developing increase of resistance. The response with which we are dealing has none of the brusque and decided characteristics of the galvanic response to nocuous stimuli; its slow and variable onset and the indefinite nature of the stimuli that tend to arouse it do not allow of any formulation of the latent period of this increase of resistance. I have never seen it occur under five seconds with the type of stimulus that I have been considering. This indefiniteness may partly be attributed to the method of experiment—to attempt to produce such a violent reaction as that which we characterise as joy is, under the conditions of the somewhat dreary experiments conducted in the laboratory, a practical impossibility. The muscular tonus response that has been found to be evoked by both effort and nocuous stimuli cannot, of course, give the same clear-cut answer as the specific galvanic reflex, but the tendency is in the same direction. When the painful stimulus is removed the muscular hypertonus relaxes slowly, and ultimately relief from pain is characterised by a far higher degree of relaxation than that found at the onset of the stimulus. This relaxation is well shown in Fig. 10. The pulse-rate becomes slower after the nocuous stimulus, and this slowing may be observed in the galvanometer curve of reaction to a pistol shot (Fig. 1). In this case, before the stimulus was administered, the pulse-rate had been more rapid than normal, and immediately after the stimulus was still further increased for a couple of beats and then becomes slower. We have here, therefore, a complex result of two different forms of excitation—the suggestion that a disagreeable experience is to be undergone, and the stimulus itself. It is characteristic of the cardiac response that its duration is almost confined to that of the stimulus itself; hence the

slowing that occurs after relief from the stimulus may be actually present while the other forms of response, such as the galvanic reflex, are still in progress. The response, therefore, to a benign stimulus is a diminution of organic activity. Philosophers of all ages have frequently drawn attention to the superior efficacy of pain as a vital stimulus. So far as an objective study of these reactions has taken us the reaction to a benign stimulus is only presented as a relief from the previous activity occasioned by a nocuous stimulus. It is not possible here to follow the line of thought suggested by these experimental results and to inquire whether benign stimuli with their pleasurable sensory aspects should not be considered merely as an interruption of the stream of nocuous impulses that spur the organism to activity. Theophrastes, quoting Anaxagoras, tells us that to feel is to suffer *ἀπασαν δόλσθησιν μετὰ λύπης*. If we substitute for the definite presentation of the specific sensation the vague affective state that accompanies a nocuous stimulus, the dictum of the early Greek philosopher holds true. Pain is the fundamental fact and pleasure nothing but relief from pain. It will be objected that moments of great joy are certainly accompanied by the exhibition of bodily activity—the winning side cheer and clap their hands—the dog will bound with pleasure when he recovers his lost master. This difficulty is easily dealt with. Such exhibitions of activity are not specific responses to the benign stimulus. They are not directed to the prolongation or the curtailment of the bodily reaction to the stimulus. They appear to be a compound of at least two factors, the discharge of certain reflex activities that have been inhibited by the tension of the muscular system, and the appearance of a specific type of nervous activity—the instinct to communicate with others.

A great deal of confusion has been occasioned by statements to the effect that the vasomotor reactions studied by the plethysmograph show an active dilator response to pleasurable stimuli which is in every sense the antithesis of the constrictor response to disagreeable stimuli. This statement, which is unfortunately copied from text-book to text-book, is based, as Shepherd has shown, on a very few experiments of Lehmann, which have not been confirmed by other observers. Using my own modification of the plethysmograph I have only succeeded in demonstrating the same type of slow return to the normal state from a vasoconstriction due to a nocuous stimulus that we have seen to occur with the galvanic response.

The objective study of these bodily responses to stimuli possessing feeling tone lends some support to the tridimensional theory of feeling of Wundt and the later somewhat similar view advocated by Royce. Without entering into any discussion of these questions it is still important for the understanding of neurotic disturbances to realise the plurality of the bodily responses that go to the make up of an affective state.

LECTURE III.

IN the preceding lecture I dealt with some of the forms of response to nocuous stimuli from a physiological point of view. We cannot, however, content ourselves with purely physiological observations. Our patients come to us complaining of certain definite subjective symptoms and our object is to detect the defects of bodily mechanism of which they are the signs. It therefore becomes a matter of urgent importance to determine so far as we can the relation between bodily responses to stimuli and affective states. It is true that we have learnt physiologically to observe only an infinitesimal part of the bodily changes that are associated with affective states; but that small part is, as we have seen, susceptible of quantitative as well as qualitative observation. As a first step we must consider briefly what we mean by an affective state and what relation it bears to sensation.

SENSATION AND AFFECTIVE STATES.

Sensation is defined as an elementary mental process which is possessed of the attributes of quality, intensity, clearness, and duration. Affection is similarly an elementary mental process, but though possessed of the attributes of quality, intensity, and duration it has been denied that it possesses the attribute of clearness. It is said to be impossible to attend to an affection. If we attempt to do so the quality of pleasantness or unpleasantness disappears and we find ourselves contemplating some obtrusive sensation that we have no desire to observe. If we want to get pleasure from a concert or a picture we must attend to what we hear and what we see. As soon as we try to attend to the pleasure itself the pleasure is gone. (Titchener.) Herein lies the pith of the argument for dissociating affection or feeling from sensation. The subsidiary argument that the opposition of the qualities of affective pleasantness and unpleasantness is not paralleled by any of the facts of sensation appears to me to be untrue, or at best unprovable, because we know no more about pure sensation than we do about pure feeling or affection.

It is at this point that objective psychology comes to the rescue. The reason for the apparent difference between affection and sensation has been made clear by neurological investigations, especially by the work of Head and Holmes. Two systems of afferent function exist—the one system reacts to stimuli of a nocuous nature, and the effector organs which manifest its activity are either organs not under the power of conscious effort or else certain combinations of reflexes which cannot be voluntarily activated. The great terminal ganglions for this mechanism are in the thalamus. This system is phylogenetically older than the cortical system. It originates the defensive reflexes by which the body reacts as a whole to nocuous stimuli, whether by glandular, visceral,

vascular, or muscular pattern reflexes. There is another system of nervous mechanisms by which appropriately adjusted reflex patterns are combined in response to stimuli not in themselves possessing either nocuous or benign characteristics, and the terminal coördinating centre of this mechanism is in the cortex. Its function is, to borrow the language of Head and Holmes, discriminatory, and this discriminatory adjustment of certain reflex mechanisms to various stimuli is correlated with consciousness.

The two systems are not, however, independent. When the activity of the cortical processes is impeded, by inhibition arising from either external or internal stimuli, an activation of the thalamic system may occur; in other words, the resources of the body as a whole are mobilised to overcome the resistance. Conversely changes of the activity of the thalamic effector organs when they reach a certain degree of intensity stimulate the cortical receptors and we become aware of a change in the common sensation of the body. The consciousness of such a disturbance constitutes what we term an affective state. This reciprocity between the effector organs of the thalamic system and the cortical discriminatory system was already clearly appreciated by Hobbes—"adeo inter se motus cordis et cerebri sunt reciproci." The function of the cerebral cortex has been said to be discriminatory, a certain stimulus or group of stimuli being integrated with a specific reflex pattern activity, but when stimuli arising from the activity of the thalamic system reach the cortex they represent changes taking place in every part of the body. No one elementary group of sensations will be prepotent; we are only aware of a diffuse sensory disturbance. Such appears to be the objective explanation of the origin of the attempt made by psychologists to differentiate between feeling and sensation. When the thalamic activity is of great intensity in response to a maximal stimulus, such as intense fear, certain of its elements may be so intense that they dwarf the remainder and are attended to as an ordinary sensation when their afferent impulses reach the cortex. Thus an absolutely definite sensation of nausea is experienced by some men when under fire, others complain of a burning sensation in the throat, others of palpitation; and it is a peculiarity of the predominant sensations that they may so dwarf those arising from other forms of organic resonance that a man who is not conscious of any great degree of fear simply becomes aware of a sensation of nausea when under fire for the first time. It may not be till after he has gone through the experience on subsequent occasions that he recognises a connexion between his nausea and exposure to danger.

It is in the preponderance of some one such type of reaction, due either to innate or acquired anatomical abnormalities, that we find the explanation of so many of the visceral types of neuroses. In many cases the actual movement of the effector organ rather than its sensory concomitant holds the attention, as in the case of the well-known occurrence of vomiting, micturition, or defæcation as a response to nocuous

stimuli. In the last lecture we have seen that the organic response to noxious stimuli is manifested as activity, and the response to benign stimuli as quiescence, and we are therefore justified in associating activity of the thalamic system with unpleasantness and quiescence with pleasantness. So far as it has been necessary to speak of these sensory concomitants of the bodily reactions I have spoken of them as states of affection or of feeling. From the physiological standpoint I can see no difference between an affective state and an emotion, and I am perfectly willing to use either term indifferently. From what can be gathered from the writings of psychologists it would appear that when certain sensory elements of an affective state sufficiently predominate so as to direct the attention overwhelmingly to their presentation the state is said to be one of emotion; the difference is therefore one of quantity and not quality. I do not propose to enter into any attempt to differentiate the various types of emotions or affective states. Much of the psychological literature on this subject is characterised by that peculiar naivete with which the scientific specialist too frequently tends to regard life. Our preceding short review of some of the objective changes verifiable as bodily responses to affective stimuli is sufficient to substantiate the acceptance of the popular psychology of "mixed feelings." We have seen that movements common to other states of activity may occur as concomitants of different affective states.

PROBLEM OF ORIGIN OF AFFECTIVE STATES.

However much we may wish to confine our study of the neuroses to a purely objective basis we are unable to evade the question as to whether an affective state is to be regarded as conditioned by the physiological changes of bodily activity, or whether such changes occur as the organic resonance to a preceding affective state. Our whole system of the interpretation of the emotional aspects of the neuroses must be influenced by our answer to this problem. Ancient writers answered it in no uncertain fashion :

*"Cor ardet, pulmo loquitur, fel commovet iras,
Splen ridere facit, cogit amare jecur."*

Aristotle and his school of course recognised no other bodily mechanism for mental processes than that of the thoracic viscera. The Stoics, for the most part, rejected the brain as the seat of mind, and Zeno, Chrysippus, Diogenes, and Apollodorus were unanimous in proclaiming the heart to be the seat of the emotions. It would be too lengthy a task to follow the causal attribution of the affections to visceral changes throughout the Middle Ages. In recent times it has been revived in the James-Lange theory of emotion. I cannot do better than give the theory as propounded in James's original words: "Common sense says we lose our fortune, are sorry and weep; we meet a bear, are frightened and run; we are insulted by rivals, are angry and strike. The hypothesis here to be defended says that this order of sequence is incorrect: that the one mental state is

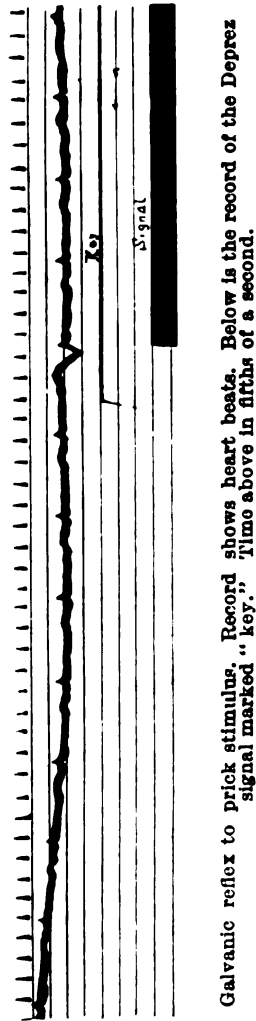
not immediately induced by the other, that the bodily manifestations must first be interposed between, and that the more rational statement is that we feel sorry because we cry, angry because we strike, afraid because we tremble, and not that we cry, strike, or tremble because we are sorry, angry, or fearful, as the case may be." This view has apparently been held in different forms by Sergi, Richet, Ribot, Münsterberg, and others, and has provoked a storm of controversy.

I shall not attempt to follow the arguments based on introspective considerations, but will turn to those furnished by objective methods. Sherrington attempted a physiological solution of the problem by depriving a dog, so far as possible, of all afferent paths of somatic sensation. He transected the spinal cord in the cervical region and subsequently performed double vagotomy. In spite of the deprivation of organic sensation that was occasioned by these measures the animal showed unmistakable signs of emotion when angered or menaced. The experiment is, as Sherrington recognises, by no means conclusive; all that it entitles us to say is that for the dog in this condition emotional manifestations were confined to the head and neck area, and we have already adduced evidence that changes in muscle tonus are just as much one of the factors of the organic emotional response as visceral and vaso-motor changes. Ward has urged that James's theory is a flagrant *ὕστερον πρότερον*—a putting of the cart before the horse. Emotion is always the expression of feeling; and feeling, for the subject that feels, has always some objective ground. Emotion is never the reception of impressions, but is always the response to them. Let us see how far a purely objective inquiry as determined by observations of the bodily reactions will help us to settle the question. Fig. 1 is the record of a reaction to a nocuous stimulus, manifested by the galvanic reflex, of a motor voluntary reaction and of an involuntary motor reaction or start. About the last-named reaction—the start—I have little to say; its latent period is very short, about 0.08 of a second. It can be, as Sherrington has shown, elicited as a purely mesencephalic reaction to auditory stimuli in decerebrate animals, when its latent period is about 50 σ . In this case the stimulus was a fainter one, and the latent period is appreciably longer than that found by Sherrington in animals—and this is the rule for any type of start reflex as elicited in man; it is therefore by no means certain that it has the same bulbar origin as the reflex in decerebrate animals. It is not an invariable accompaniment of affective states determined by nocuous stimuli, and for our present purpose we may disregard it. The next event recorded on the photograph is the voluntary motor reaction: the subject was instructed to press a key as soon as he perceived a prick. The latent period is here a normal one of 0.2 second. The third event is the movement of the galvanometer fibre at the beginning of the galvanic reflex. The latent period of this reflex is here 2 seconds. If the galvanic reflex be taken to indicate one of the many bodily responses that go to make up the general state of bodily activity

whose sensory equivalent is an affective state then this affective or emotional state is arrived at quite 1.8 seconds after the initial stimulus has been perceived and acted upon.

It might be urged that the galvanic reflex is a response sui generis with a remarkably long latent period, and that the other responses take place more rapidly. The analogy between the galvanic reflex

FIG. 1.



and the time relations of the "cat pad" phenomenon of Luchsinger might prima facie lead us to the same conclusion. The experiment of Luchsinger, it will be remembered, consisted in observing a secretory current from the pad of a cat's foot when the sciatic nerve was stimulated electrically and the latent time of this reaction, measured by Waller in the human subject, is about 2 seconds. The latent period of

the plethysmographic response can be measured with a fair degree of accuracy, and in the previous lecture we have seen that its time relations are the same as those of the galvanic reflex. The latency of the alterations of pulse rhythm cannot obviously be determined accurately, but by collation of a large number of tracings I have never found it to be a shorter period than 2 seconds. We have seen reason to believe that the acceleration of the cardiac rhythm is due to removal of the inhibitory action of the vagus, and physiological experiments assign a latency of about 1 second to the vagal reflex.

The latent period of the respiratory changes is similarly incapable of accurate determination, but I have never found it to be less than 1 second. The muscular tonic response in the majority of my determinations had a latent period of about 2 seconds. I have no data as to the latent period of visceral and glandular activity, but indirect evidence would point to their being at least equally long. Thus the objective evidence is unequivocal—the stimulus is perceived, differentiated, and acted upon a considerable time before the presentation of the sensory concomitants of the bodily reactions could be experienced as an affective state. In my own case introspection seems to confirm the objective data. Experiences in the line in France were perhaps a little too complex for analysis, but in the streets of London my absence of mind has frequently nearly involved me in a motor accident. In such cases after successfully avoiding the oncoming vehicle I have experienced some 2 seconds later the feeling that we used to call as children "going hot all over." Had the stimulus been less transitory and the motor pursued me instead of avoiding me the continued organic response would on the sensory side have amounted to what we know as a state of fear.

POSSIBILITY OF EXISTENCE OF AN OBJECTLESS AFFECTIVE STATE.

It is of great importance for the understanding of the nature of neuroses that we should determine whether a reversal of this normal sequence of events can take place; that is, can a pre-existing state of bodily activity, which is the physical aspect of an affective state, determine the orientation of cortical activity so that the state of emotion arises first, and then an object is assigned to it? It may be disputed whether an objectless affective state can exist, but there is ample evidence that the existence of the bodily concomitants of an affective state will facilitate the representation of some situation which will then be assigned as its object. Marañon injected a small dose of adrenalin into a sensitive patient, and obtained various subjective sensations which as a rule constitute the syndrome of terror. At times this was noted by the patient himself, who declared: "I feel as if I were afraid, but I am calm." When, however, he supplied an appropriate verbal stimulus by mentioning some source of anxiety to the patient, although such a stimulus would naturally have caused but little

reaction under normal conditions, the patient would break down completely in a fit of emotion.

Hitherto I have not dealt with the influence that may be exercised on the response of the nervous system through the agency of the internal secretions.

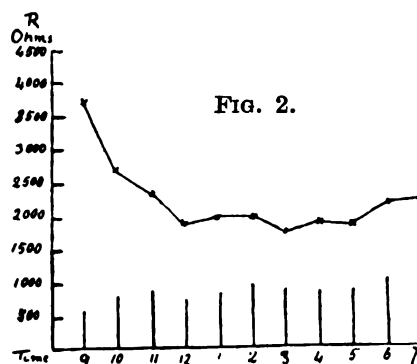
DISTURBANCE OF ENDOCRINE SECRETIONS IN RESPONSE TO NOCIOUS STIMULI.

The classical experiments of Cannon seem to have demonstrated that states of excitement are accompanied by a hypersecretion of adrenalin, as evidenced both by direct serum tests for its presence and by the occurrence of glycosuria. His brilliant demonstration has been received with great enthusiasm and a far greater rôle has been assigned by the uncritical to the part played by the hormones in the activity of the nervous system than can be justified by observation. It is too readily forgotten that the effector organs of the vegetative nervous system respond to the internal secretions of the adrenals in precisely the same way as they would if acted upon by the vegetative system directly. It is therefore no proof that a reaction is due to the stimulation by an internal secretion, and not to the autogenous activity of the nervous system, to say that the reaction resembles that which is experimentally produced by the injection of the hormone. Swale Vincent has pointed out that there is no evidence whatsoever that adrenalin, for example, is a normal constituent of the blood; indeed, there is much cogent evidence against such an argument.

That under certain conditions of great excitement adrenalin may be present in the blood seems to be fairly well established from the work of Cannon, but were it secreted as a response to stimuli of a less intense and prolonged nature it could only be present in the blood in such minute amounts as to be incapable of initiating the bodily emotional responses. I have conducted a series of observations on my own blood taken before and after the experience of ten minutes' faradisation. In no case was I able to detect any hyperglycæmia as a reaction to the pain stimulus. It is obvious that the painful stimulus was inadequate inasmuch as it neither increased the blood sugar nor produced glycosuria, but the pain was certainly more severe than is likely to occur in the normal experience of healthy life, and it seems legitimate to assume that the ordinary noxious stimuli of daily life are unlikely to affect the secretion of adrenalin. This criticism applies even more strongly to the internal secretions of the other endocrine organs as a direct response to noxious stimuli. When we turn to the evidence in support of the direct influence of the internal secretions on the threshold excitability of the thalamic system, we are on surer ground. There is ample clinical evidence of the state of hyperexcitability of patients suffering from hyperthyroidism to stimuli adequate to arouse an affective response. Experimental observations show that the hormone of the thyroid has a marked influence on bodily activity. This hormone has been isolated and identified by Kendal as an indoxyl

iodine compound and found by him to raise the rate of basal metabolism 2 per cent. in a man weighing 70 kilos. when administered in a dose of 5 mg.

I have in a previous lecture dealt with the diurnal variation of the bodily resistance described by Waller, and I showed that there was evidence of a rough correspondence between the magnitude of the galvanic response and the diurnal resistance variation. In order to test the action of ingested thyroid gland on the galvanic response I again made use of this diurnal variation. By taking large doses of thyroid in the early morning I was able both to diminish the mean value of the skin resistance and to mask its diurnal variation. At the same time the galvanic response to uniform sound stimuli of moderate intensity was markedly increased. Fig. 2 may be compared with the record of the diurnal variation of resistance and the magnitude of the galvanic response represented



Above, curve of diurnal resistance as altered by ingestion of thyroid extract—compare Fig. 8, Lecture II. Below, responses $\times 2$ to maximal stimulus (pistol shot).

by Fig. 8, in the second lecture. Each diagram represents the mean observations of three successive days. Subjectively, whilst under the influence of thyroid in large doses, I was aware of a marked degree of irritability which lasted throughout the time of the thyroid ingestion experiments, but which appeared to be accompanied by a rather increased power of doing work. I give these subjective observations for what they are worth. That a diminished skin resistance occurs in cases of exophthalmic goitre was shown long ago by Vigouroux. The action of adrenalin in producing effective states has already been considered; but in the absence of any proof of its normal presence in the blood stream we have no right to consider that the normal activity of the affective thalamic mechanism is influenced thereby. There is some direct evidence that the internal secretions of the gonads facilitates the specific affective response to sexual stimuli as shown by the results obtained with implantation of testicular grafts in man and animals suffering from loss of sexual desire. Although there is every reason to believe that the internal secretions of other glands have a direct influence on the affective responses

it is difficult in the present state of our knowledge to bring forward any incontrovertible proofs of this hypothesis. It must never be forgotten that a glandular structure in the normal body is not inert so far as the furnishing of afferent impulses to the central nervous system is concerned.

It may well be that these afferent impulses and not the internal secretions evoked by their activity are the determining influences of the glands on any particular mechanism of response. I was able to obtain records of the secretion of saliva from my own parotid gland by applying a small catheter tube maintained in position by a suction ring over the orifice of the duct. This procedure has been adopted by other observers for the recording of conditioned reflexes produced by the sight of food; I found that nocuous stimuli, if of sufficient intensity, tended to produce inhibition of the saliva flow. The fall of the drops was recorded by allowing them to tilt a tipover key that closed a Desprez signal circuit and thereby recorded on a smoked drum. There is not wanting evidence of the disturbances of the gastric, intestinal, and renal secretions as a response to nocuous stimuli. We have so far seen that the mechanism of all forms of cerebral activity is capable of being recorded in terms of muscular and glandular activity; before attempting to transfer this knowledge to the investigation of neuroses we must consider the constitution of some of the more complicated nervous mechanisms in their barest outlines. In the last lecture I showed a slide (Fig. 7) illustrating a conditioned reflex; you may perhaps remember that the subject was taught by means of a painful stimulus to perform a certain movement and that we noted that when the stimulus was intermitted, whilst the audible sign that had hitherto accompanied it was made, the subject responded precisely as if he had perceived the stimulus. We also noted that the signs of an affective response, as evidenced by the galvanometer, were present when the click of the electric key occurred in the absence of the stimulus. In the language of popular psychology the subject had formed a habit, or in that of physiology a pattern reflex had been conditioned. Now supposing the stimulus had been repeated a requisite number of times, the subject would, at any rate for the first few occasions on which the click of the key was alone given, have found himself utterly unable to control the movement of pressing the signal key. But this movement was in the first instance one that had been acquired as a result of the activity of the discriminatory mechanism of the cortex. It has now ceased to be discriminatory and become independent of the first process of nice adjustment of a specific mechanism to a specific response by the inhibition and coördination of other forms of cortical activity. There is, however, no evidence that the response has ceased to be controlled by the same cortical mechanism which started it. I found in this particular instance that after the first few times the voluntary muscular reaction settled down to a constant latent period of 0.18 second and that later when the conditioned reflex was elicited by a click alone the latent period

remained unchanged. Owing to the slow rate at which these particular records were taken the latent periods could not be read closer than to 0.02 second, but the accuracy is sufficient to justify our assumption that the reaction continued to be performed by the same cortical mechanism that had been responsible for its initial manifestation.

Now this statement embodies a very important fact of which the psychotherapist endeavours to make full use. It means that when the reaction had become part of a conditioned reflex and had ceased to be the centre of conflicts between various alternative reflex paths, which conflicts we generally associate with conscious perception, the conditioned reflex still made use of the same cortical mechanism. That is, it still had a direct nexus with all those processes with which it had been originally connected. Therefore by the use of appropriate methods of observation it should be possible to determine what the original associations were when they are no longer objects for the subject's own consciousness.

CONDITIONED REFLEXES IN DAILY LIFE.

Now the greater part of our daily conduct is made up of such conditioned reflexes or habits, and the more effectively they have been established by constant repetition the more difficult it is to interrupt the reflex pattern by some fresh stimulus. We defined one of the attributes of a noxious stimulus as a tendency to interfere with and impede the normal tendencies of vital activity. There is no more fixed or powerful activity than that of a well-established habit mechanism. A verbal or physical stimulus that impedes the activity of a habit reflex pattern will therefore act as an intense noxious stimulus, and through the inevitable thalamic mobilisation of the bodily activities to resist such interruptions an intense affective state will be the sensory result. Not only stimuli from outside may tend to impede the activity of the habit mechanisms. Attempts on the part of the subject to interfere with them will equally evoke the generalised bodily response with the corresponding unpleasant feelings. Lastly, the constant occurrence of these reactions, whenever the habit mechanism is interfered with, may in itself condition a new reflex pattern—an active opposition to all attempts to cause the feeling of discomfort by interfering with the primary habit. Such, I believe, is a restatement in the language of objective psychology of the rather clumsy symbolism which the psycho-analyst makes use of; such terms as “the censor” would appear to be unnecessary in this connexion. There is another type of pattern reflex even more potent and more dissociated from the discriminatory mechanism of the cerebral cortex. Unlike the conditioned reflex it has never arisen in the life of the individual from a discriminatory response to a stimulus. This mechanism is an inherited one, and is unchained by some one specific type of stimulus and by no other. Such innate reflexes of a specific type are in greater or less degree common to all the individuals of the

same species; these inherited reflex patterns are known as instincts.

INSTINCT REFLEXES.

Now by definition an instinct is an inherited pattern reflex. It is evoked by a specific stimulus and in response to this stimulus the pattern is unfolded. The end-result of the reflex is implicitly determined by the nature of its innate mechanism, and it is a mere matter of chance whether this end-result is ever presented to the subject who owns the reflex. Though by observation we may sometimes learn what the end-result really is, it by no means follows that we shall necessarily do so, and in the case of the lower animals—as when an insect, after laying its eggs, prepares food for larvæ that it will never live to see—it is quite certain that it can never know the end-result towards which the instinct reflex is orientated. Now it is of great importance to the understanding and treatment of the neuroses that we should know whether an instinct reflex has any such relation with other discriminatory mechanisms as may allow us by association methods to determine its true orientation. We may recognise that a certain line of conduct is not substantially in harmony with the environment, that attempts to impede it cause great emotional disturbance, that its origin is obscure and its end-result opposed to the interests of the patient. It is, however, only by tracing some affinity between its mechanism and the nervous system as a whole that we can hope to understand or influence it. In the case of a habit or conditioned reflex this is relatively easy. It arose as a discriminatory response to a certain stimulus—that is, it was once an object of experience and may again be recalled by appropriate methods. But if the instinct be an inherited mechanism, how can its origin be with any certainty deduced from its relation to other mechanisms accessible to consciousness? The problem is a fundamental one, and has presented itself in many forms.

To the Atomists, to Heraclitus, and to the Pythagoreans (who never drew a distinction between animal and human intelligence) the problem was never presented, nor do we see any trace of it in the anthropomorphic animal psychology of Plutarch. The conception of a divergence between abstract thought and animal life is implicit in Plato, and the distinction became more definite in the writings of Aristotle and the Stoics. In scholastic thought we find instinct formally recognised as comprehending the totality of animal behaviour and the baser part of human conduct, whilst in Neo-Platonism there is a reversion to the standpoint of the Epicureans. With the wane of scholastic thought the tendency to the anthropomorphic view of animal behaviour has persisted till the present day. Darwin formulated our present knowledge of instinctive behaviour and gave full recognition to its recurrence in man and its evolutionary significance.

The problem as to the relation of instinct and intelligence now becomes a biological one. Those who hold the Neo-Lamarckian doctrine as to the

hereditary of acquired characters may consider that instinct is nothing else than a hereditary conditioned reflex—that somewhere in the past a discriminatory action became a conditioned reflex, and by the aid of natural selection such a conditioned reflex has been handed down as an innate part of the nervous mechanism. If an instinct in its earliest stages originated as an act of conscious discrimination its later hereditary form will still show some affinity to the conscious mechanism that first started it, and we might hope that by learning something of its cortical connexions we would arrive at its origin. On the other hand, if an instinct be regarded as a variation preserved by process of natural selection, it is clear that to seek its early cerebral connexion is futile, and if we disbelieve in the heredity of acquired characters the instinct reflex pattern must be unfolded *de novo* in each generation, and the associations that it may possess will only be such as may have been acquired during the life of the individual. Men of such different schools of thought as Ziegler, Haeckel, Spencer, Wundt, Semon, Ward, McDougall, and Preyer, adopt the Lamarckian standpoint; Driesch and notably Bergson represent a return to the scholastic view of instinct. For Bergson instinctive behaviour represents a form of activity to which there can never be a psychical correlation in the terms of human practical intelligence. Human intelligence is so developed and so limited as to enable us to adopt mechanical aids to life, and therefore postulates at the beginning of any action a more or less clearly defined conception of what its end is to be. Instinctive behaviour knows nothing of ends; it can only reply to introspection in the words of Luther, "Ich kann nicht anders."

I venture to think that all speculations about the psychical aspects of instinctive behaviour founded on animal observation are of very doubtful value. The supreme act of faith is the attribution of consciousness to our fellow beings, for knowledge of consciousness is never immediately given; but to proceed to speculate about the psychical correlations of instinctive behaviour in insects can hardly be helpful to objective psychology. We must turn to human instincts, and we must obviously select for study of instinctive behaviour an act performed for the first time and from which mimicry and verbal suggestion are excluded.

EXPRESSION OF THE ANIMAL NEST-MAKING INSTINCT IN HUMAN BEINGS.

Some years ago I observed what has always seemed to me to be a singularly interesting and beautiful instance of instinctive behaviour that fulfils these postulates. If it has been already noted by others I must apologise for presenting it under the guise of a new observation. A primipara about two days before the birth of her child worked very hard at tidying not only all the drawers of her bedroom and boudoir but also her husband's desk. Asked why she did this she said that as she was going to be ill for

a long time she wished to have all her own and her husband's things in perfect order. The answer seemed to me to be somewhat inadequate, since as a rule the husband's desk was never interfered with. Some time later the father of several children remarked to me that he always knew when a birth was due, since for a couple of days before it his wife in an excess of energy would tidy every drawer she could find including all his private papers. When I asked him why she did so he said that she gave him the same explanation as I had received in the first case. Now I knew this lady sufficiently well to feel sure that on the occasion of her long absences at her country house, where she spent many months every year, the last thing that would occur to her would be to prepare for her absence by such a minute ransacking of drawers that are as a rule outside her province. I then asked a midwife if this procedure was a usual precursor of childbirth. She said that she had observed it in quite the majority of her cases, and inasmuch as her practice lay among some of the wealthiest people of the country in whose houses such duties as the arrangement of drawers and cupboards are seldom performed by the mistress the phenomenon was all the more striking. Later on when observing the behaviour of a doe rabbit in a breeding hutch I noted that for three or four days before delivery the doe spent her time in a state of frantic activity collecting bits of hay, tossing them up to unravel them, and finally carrying them to the dark compartment at the end of the cage. She was making a warm nest for the expected young. When we find that this nest-making behaviour is universal among the higher apes I think that we are entitled to assume that the drawer-cleaning, sorting, and tidying are the expressions of the animal nest-making instinct.

We have here an instinct untainted by any possibility of mimicry, and since its existence is apparently unknown, free from any complication due to suggestion. The purpose of the reflex instinct mechanism is unknown to the expectant mother, and when her attention is directed to it, and she is asked what she is doing, she casts about for an explanation and evolves one that is not only false but shows no associational nexus to the true purpose of her activity. The distinguishing feature of an instinctive reflex is its compelling urgency. The least delay or opposition to its accomplishment, once it has been aroused by the appropriate stimulus, evokes an intense bodily reaction, and it would appear to be of the imminence of such an explosion of feeling that we speak of as a feeling of compulsion. This feeling of compulsion is the real equivalent of what Bergson terms intuition in respect to instinctive activity. Like the Bergsonian intuition, it cannot be translated into the language of practical thought, nor has it association of a direct nature with aught other than the immediate instinct mechanism. These innate pattern reflexes that we term instincts undoubtedly play an enormous part in the mechanism of conduct. Their recognition in all but such simple cases as I have just now narrated is a matter of great difficulty. They can as a rule be

only distinguished from the conditioned habit reflexes by a minute knowledge of the subject's past history such as neither he nor the observer can hope to possess. Much of the vast output of writings on the subject of the instincts that has been characteristic of the last few years loses considerably in value on this account. As I am concerned only with an attempt to show what fundamental knowledge concerning organic disturbances of mechanism can be gained from an objective study of bodily responses and of conduct, I will make no attempt to deal with any system of classification of the different forms of instinctive mechanism. There appears to be a tendency to over elaboration in this direction—*Essentia non sunt multiplicanda praeter necessitatem*—the "razor" the "doctor invincibilis" has its application in psychological medicine as well as in philosophy. One particularly deplorable move in this direction has been the invention of states or attitudes to take over the very attributes without which an instinct cannot be recognised as such. Thus to account for the compelling power of the instinctive mechanism that will drive a man into courses of conduct that are directly at variance with his interests in society as at present constituted, we are invited to divest the instinct of its compelling power and to lay it at the feet of an entity termed the "self regarding sentiment" for whose satisfaction we yield to the unprofitable enterprise. There is a flavour of mid-Victorian self-righteousness about this sentiment; it may possibly have been of great usefulness in strengthening the resolutions of conscientious objectors, but the men who sacrificed their interests in the war because they felt that they could not do otherwise had little use for it. The modifications that will be imposed on a primary instinctive mechanism by the pressure of the environment will be incalculable. It is for this reason that in the elucidation of both instinctive reflexes and conditioned habit reflexes their affinities to the affective states are likely to afford a truer if less detailed insight into their nature than any attempt to range them in a tentative scheme of classification.

From what has been said of the relations of bodily response to nocuous and benign stimuli it is obvious that I must consistently range the processes of activity that are distinguished as appetites as being nothing other than responses to nocuous stimuli. From the objective point of view such activities are the response to the present situation of pain and not the pursuit of pleasure. The satisfied man can have no appetites. The nocuous stimulus that arouses our activities is not that conditioned by the desired object itself, but by the limitations imposed by the environment that impede the possibility of our satisfaction by its possession. What is true of appetite is true of desire. As Spinoza remarks, there is no difference between appetite and desire except in so far as the latter implies consciousness. Desire is self-conscious appetite.

LECTURE IV.

IN the preceding lectures I have endeavoured to give some account of the objective features of the fundamental mechanisms of cerebral activity. I propose in this concluding lecture to indicate in what fashion objective psychology may be applied to the study of the neuroses. We have seen that the mechanisms of cerebral activity are fundamentally of two characters. In the first place the discriminatory cortical activity finds its expression in the movements of the voluntary nervous system—that is, in actual muscular movement and in the kinæsthetic representation of such movements in the motor cells of the cortex. In the second place the general reactions of the organism to stimuli that tend to destroy or impede functional activity find their expression in the movements of the thalamic system and effector organs. Since the nervous system is an instrument of movement, and nothing else, we should be prepared to find that a certain group of the functional disturbances that we term neuroses would be the expression of some chemico-physical changes affecting movement of the neurones generally. Our knowledge of the chemico-physical processes that constitute activity of the neurones is as yet too incomplete to furnish a secure basis for a descriptive pathology.

THE FUTURE TASK OF NEUROLOGY.

At present we rely chiefly on deductions from the similarity to certain aspects of neurosis in the behaviour of the organism when functional activity is disturbed by toxic substances, whether ingested or manufactured, in the body. The study of these physico-chemical disturbances will be the great task of the neurology of the future. The researches of Sir Frederick Mott and his pupils have broken new ground in the elucidation of the micro-chemical signs of disturbances of the function of the neurones, whilst the work of Pighini has opened the path for chemical investigation through the study of metabolic disturbances. The policy of the London County Council in giving effect to the scheme endowed by the late Dr. Maudsley in founding a school and hospital for the study of the earliest stages of nervous disturbances is justifying itself by the additions now being made to our knowledge of the chemical and physical changes that express disordered function of the neurones. The work of Koch and Sydney Mann performed in the L.C.C. laboratory suggests that the general bodily deficiency of oxidation activity demonstrated in dementia præcox is the interpretation of the micro-chemical changes shown by Mott to be characteristic of the nerve cells in this disorder. Just as such an advance in our knowledge of the physical basis of this form of insanity must once and for all dispose of the theories of its psychogenic origin such as that advanced by Jung, so we may hope that by similar

methods the physical basis of the asthenic forms of neuroses may be established.

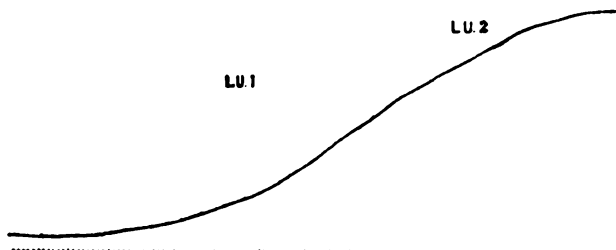
There is, indeed, a certain body of physiological evidence in favour of the view suggested by the microchemical methods of Mott and his pupils, that the processes of nervous activity are of the nature of a catalytic phenomenon. Brailsford Robertson repeated an earlier observation by Loeb and Koryanyi on the determination of the curve of the velocity with which a simple movement of drawing a straight line of indeterminate length is performed. Robertson ruled straight lines with a form of apparatus allowing the construction of a curve of the velocity with which his pencil travelled at any moment of the drawing. The pencil, which was in reality a metal stylus connected with one arm of the circuit of a battery activating a Deprez signal, travelled across a number of longitudinally arranged alternating slips of ebonite and copper. The copper slips were each connected with the other arm of the signal circuit. When the stylus travelled over one of the copper slips the circuit was closed and the signal made a mark on the smoked paper of a drum rotating at uniform speed. Since the copper slips were equidistant it is obvious that by measuring the distances between the signal marks on the drum it was possible to ascertain the velocity with which the stylus moved at any point of its journey. These data furnished a curve of the velocity which showed the following characteristics: The velocity underwent progressive acceleration; beginning slowly, the velocity of the stylus reached a maximum and then again diminished, so that the commencement and termination of every curve was asymptotic.

In order to verify the conclusions of Robertson I arranged an endless band of linen revolving with constant velocity round two drums set horizontally at a distance of about two feet apart. The band of linen was a yard in width. Midway between the two drums it passed over a third roller. The apparatus was covered by a board except for a gap about 2 inches wide just over the middle roller. A line of arbitrary length was ruled with a pencil along one edge of the gap and the quickly moving band did not allow the curve traced to be followed by the eye. No attempt was made to determine voluntarily either the velocity with which the line was drawn, or its length, so long as it was within the limits of the band. Lines were drawn both towards and away from the body, using movements of the whole arm, elbow-joint, or wrist in order to eliminate the possible influence of the type of movement employed on the form of the curve. When the band was removed the resulting curves in every case agreed with that constructed by Robertson (Fig. 1). Now Robertson has shown that such a curve is typical of an autocatalytic process—that is, a chemical process of such a nature that it is catalysed by one of the products of reaction; in such a case the commencement and termination of the velocity curve is asymptotic.

Examples in chemistry of such autocatalytic reactions, in which one or more of the products of reaction

accelerate their progress, are furnished by the hydration of methyl acetate or the hydrolysis of cane sugar at 100°. In such a reaction a point must be reached when the decrease in the active mass of the reacting substance balances the increase of the active mass of the catalyser. A catenary reaction is the only other type of reaction that will show a similar acceleration, but the autocatalytic reaction is distinguished

FIG. 1.



Curve traced by drawing a straight line across a rapidly-moving linen band. Time below in 1/100 second.

by the fact that its curve is symmetrical. The integrated equation for such a curve will be—

$$\text{Log } \frac{x}{A-x} = K (t-t');$$

where A expresses the total transformation at completion of the process, K is a constant expressing the velocity of the process, and t' is the time at which the mass of the product equals $\frac{1}{2}$ A.

CORRELATION OF CATALYTIC REACTION WITH DEFECTIVE OXIDATION IN NERVE CELLS.

Now the importance of this observation lies in the evidence that it affords that the neural process conditioning the movement is in the nature of a catalytic reaction. The researches of Mott have shown that the nervous asthenia of extreme forms of myxœdema and of dementia præcox are associated with evidences of defective oxidation processes in the nerve cells, and the correlation of the two observations affords an alluring hypothesis. The casual drawing of a straight line affords a very good example of a cortical mechanism, unchained in response to an autogenous voluntary stimulus, which runs its course without further interference. We may look to observations of disturbances of the catalytic process such as those furnished by Koch and Mann in dementia præcox to afford an insight into the asthenic types of neurosis. The slide shows the rapid exhaustion of a patient who suffered from lack of power of concentration and a distressing sense of mental fatigue when he was set to obtain a record with the Mosso ergograph. That the fatigue was not peripheral was shown by the absence of signs of muscular fatigue in response to electrical stimulation before and after the ergographic tracing. By correlating my method for the estimation

of the effort tonus reflex, described in the first lecture, with observations on the squeeze exerted on a dynamometer I have noted that in such patients the bodily response of effort dies down rapidly, and simultaneously with the maintenance of the squeeze. The effort is, however, there, and this serves to differentiate this class of patients from those that we shall consider later under the category of hysterical weakness. It is in the treatment of these asthenic patients that so much harm is wrought by attempts to stimulate them to greater efficiency without first restoring their bodily condition.

NECESSITY OF CONSTITUTIONAL TREATMENT OF ASTHENIC PATIENTS.

All neurologists of experience are convinced of the great efficacy of constitutional treatment which is too often ignored by the new school of psychotherapy. I will now turn to consider those neuroses in which the predominating symptoms are manifested objectively and subjectively as an excessive response on the part of the mechanism that we have studied as the bodily reaction to nocuous stimuli. I have endeavoured to show that the bodily response to nocuous stimuli is essentially one of activity, and that the benign or agreeable stimuli are responded to by quiescence; and, furthermore, that the activity which we occasionally ascribe to the action of agreeable stimuli is really the response to those conditions of the environment that hinder their enjoyment. The time at my disposal would not allow me to attempt to consider in detail the various forms in which such a hyperexcitability of the mechanism of affection may show itself.

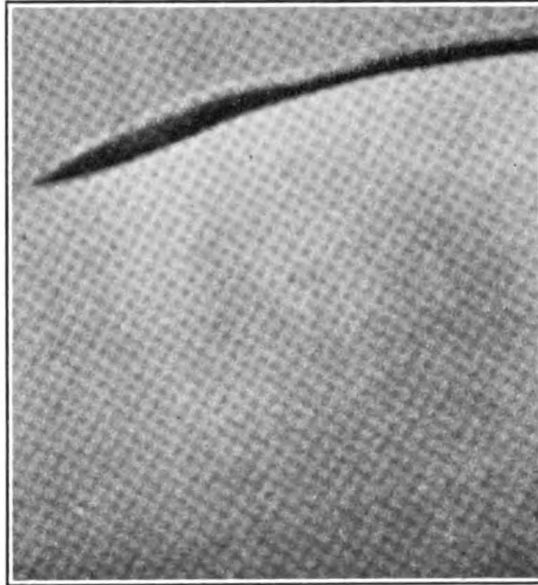
In the previous lecture I spoke of the caution with which we must view all attempts to attribute activity of the vegetative nervous system to the direct action of the internal secretions; it is much more promising to seek for evidence of modifications of the excitability of the autonomic mechanism as a result of long-standing hyper- or hypo-function of the endocrine system. The relations between excitability of the autonomic system and glandular activity have been more extensively studied in the case of the thyroid than in that of any other gland; I will not dwell on the well-known symptoms of hyperthyroidism; there are, however, a certain number of cases of neurosis exhibiting a hyperexcitability of the affective mechanism together with tachycardia, vasomotor disturbances, and tremor without any thyroid enlargement. There are three signs revealed by the objective examination of such cases on which I lay great stress. First, the hyperexcitability of the mechanism of affection as revealed by a study of the galvanic reflex; in these cases the skin resistance is invariably very low. This sign, though never absent in indubitable cases of hyperthyroidism, can, of course, taken alone, only amount to an objective demonstration of the hyperexcitability of the affective mechanism. The isolation of thyroxin, the active principle of the thyroid internal secretion, has permitted the quantitative

estimation of the influence of the thyroid on metabolic activity. Since in cases of indubitable hyperthyroidism we invariably find the basal metabolism to be above the normal rate we cannot diagnose its presence in the absence of this sign. The determination of the rate of basal metabolism is a procedure of no great difficulty, which can be accomplished in a very short time with fairly simple apparatus. It is to be hoped that this valuable method will soon become an established procedure in the investigation of cases of neurosis. There is, however, a third sign of the existence of the condition of hyperthyroidism which is likely to prove of great value. Goetsch has devised an intradermic test that serves to demonstrate the existence of hyperexcitability of the sympathetic system. The reaction depends on the demonstration of sympathetic hyperexcitability by injection into the superficial layers of the epidermis of minute quantities of adrenalin. The test shows no more than that the sympathetic system is hyperexcitable, and furthermore it only demonstrates a hyperexcitability at the junction between the sympathetic neurone and the effector cell. It cannot, therefore, be held to be of absolute diagnostic import, any more than the exaltation of the galvanic reflex. Its importance lies in the fact that it is apparently never absent in cases of hyperthyroidism, and taken with the two preceding tests it will establish the diagnosis. As modified by Ascoli and Faggioli, the test is described thus: When 0.05 c.cm. of a 1 per 1000 solution of adrenalin is injected by a fine hypodermic needle, pushed just under the epidermis, so that its whole intradermic course is clearly visible through the skin, the resultant swelling assumes after a few minutes a dark-blue colour as if ink had been injected. The swelling then becomes surrounded by an alabaster-like halo which grows in intensity and extent, often sending out irregular shoots in one or more directions. Around the white halo appears in turn a red halo, more or less intense in colour and width. Frequently a contraction of the pilomotor muscles occurs, giving an appearance like goose flesh to the alabaster zone. This is fairly well shown by the photograph (Fig. 2). The area of goose flesh in my photograph is not, however, limited to the alabaster zone. Having reached its maximal development in half an hour, after a stationary period of an hour or so, the reaction gradually disappears, the blue spot changing to red, and leaving ultimately a small swollen papule. By using a more dilute solution, for instance, one in two hundred thousand to one in a million, the reaction is less intense but always preserves the same type. It differs, however, by the absence of the central blue spot for which a small red mark is generally substituted later on, and the red halo is not always prominent. The excitability of the subepidermal test in ordinary circumstances lies between dilutions of one in two hundred thousand and one in a million (Parke Davis phials). In some cases of disturbances of the menopause, of arterial hypertension, of Graves's disease, and sometimes in pregnancy, the excitability is increased, giving positive results with further

dilutions up to one in five to twenty millions. It should be always compared with a control injection of distilled water, as some people react in a somewhat similar fashion to the water injection.

Using this technique in preference to that of Goetsch I have obtained positive results in all those of my cases exhibiting indubitable symptoms of hyperthyroidism with hyperemotionalism, and in some dozen cases occurring at the climacteric in which flushing, giddiness, and nervous tremors were complained of, and which showed an excessive galvanic reaction. So far the evidence seems to be clear that hyperactivity of the mechanism of affection is associated with the frequent occurrence of hyperactivity

FIG. 2.



Intradermic test for sympathetic hyperexcitability, showing the needle track and an appearance like goose flesh in the alabaster zone.

of the thyroid. That thyroidism is not the only cause is certain; we find such hyperexcitability associated with other bodily states, in diabetes, at puberty, at the climacteric; it can be produced artificially by many drugs such as adrenalin. That hyperthyroidism can be conditioned by the environment is certain; cases occurred during the war in which pronounced symptoms of Graves's disease were noted within a few days of exposure to the strain of action; but I have already sufficiently emphasised in my first lecture that considering the multitudes subjected to like conditions we cannot but come to the conclusion that

the very small number of men affected had a pre-existing abnormality of the thyroid function. There is good reason to believe that a long-continued excitation of the affective mechanism may lead to a temporary hypertrophy of the thyroid activity; this fact was demonstrated by French observers in the civilian population of bombarded towns, but where there is no pre-existing state of organic instability such states are not lasting. The implantation experiments of Steinach have demonstrated that excitability of the affective mechanism subserving sexual activity may be directly influenced by the internal secretions of the gonads.

PROBLEM OF RELATIONSHIP OF INTERNAL SECRETIONS TO NERVOUS MECHANISMS.

Our knowledge of the relationship of other internal secretions to nervous mechanisms is as yet too scanty for discussion; such secretory activity may well be the determining factor in unloosing innate types of nervous mechanism or instincts—e.g., the unchaining of the dormant maternal instincts in the capon. Some of the wildest imaginings of the novelist may, indeed, have a basis in physiological fact. It is by no means inconceivable that latent innate reflex patterns may occasionally be aroused without any form of suggestion by knowledge or example on exposing the individual to the appropriate environmental stimulus; examples are not wanting in the study of animal behaviour. The mention of these abnormalities of instinctive behaviour leads us to the consideration of another type of neuroses, in which the distinguishing feature is some line of conduct, which is at entire variance with the demands of the environment and which we can recognise to be related to the affective symptoms that are aroused by any interference with it. We have already seen that it is hopeless to seek in such conditions for associations between the primitive innate mechanism and conscious discriminatory processes. These types of instinctive behaviour may occasionally have been re-awakened by the environment, or they may owe their appearance to certain structural abnormalities which constituted the primary stimulus at a period when the innate mechanism was not at variance with the more primitive conditions under which the ancestral stock lived. It is only the manifestation of primitive instincts that are ill-adapted to the environment which is of importance to neurological medicine. Similar in their manifestations to the instincts, and yet so different in their origin, are the conditioned reflex patterns or habits. Both types have, as we have seen, this in common, that interference with their free activity is responded to by the nervous system in the same fashion in which it responds to a noxious stimulus which tends to injure or impede the normal course of vital activity. The resultant powerful bodily reaction with its disagreeable affect may on frequent repetition condition a new defensive habit mechanism of which certain writers who prefer the

terminology of dynamic symbolism speak of as repression by a censor whose habitat is the unconscious. In normal people, whose mechanism of affective reaction is not hypertrophied, such unfitting instinct and habit mechanisms will cause but little disturbance. In those whose affective mechanism is hyperexcitable the disturbance produced may be so profound as to affect every manifestation of conduct. What is in some men an eccentricity constitutes in others a neurosis.

PROBLEM OF STIMULI ORIGINATING HABITS.

Now though to endeavour to discover what are the primary psychical correlatives of an instinct mechanism is to attempt the impossible, to determine the form of stimulus that originally conditioned a habit is a more hopeful task; by doing so we may be able to introduce the links of the habit mechanism to other and more rational associations and so to disintegrate its power. It is this task that is attempted by those who try to arrive at the original condition by the analytic method. I do not propose to discuss the utility of the psycho-analytic method. That it has given much valuable information in the realm of psychology is beyond question; whether its application in the field of medicine has yielded advantages outweighing its manifest drawbacks is a question about which there is much difference of opinion. An attempt to discover the associations presumably existing between different processes of cerebral activity and a particular disordered mechanism by learning from the patient what he can tell of the associations which are most readily evoked by an appropriate verbal stimulus is of course a perfectly legitimate objective method, but in an attempt to base our study of neurosis on purely objective investigations we are bound to scrutinise very carefully the validity of the means which we adopt.

DIFFICULTIES OF INQUIRY BY METHOD OF ASSOCIATION.

There are several factors involved in an inquiry conducted by the method of association that must prove to be very grave difficulties in the path of anyone seeking to conduct investigations in the spirit of objective science. These difficulties are probably quite well realised by the many acute intellects that have busied themselves with the analytic method, but to recognise a difficulty is not always to be able to avoid it. The chief source of error in such investigations must always be the possibility that the subject derives his associations not from endogenous sources but from the investigator. The most casual perusal of the literature of psycho-analysis must convince any unprejudiced observer of the reality of this difficulty. We find that different investigators tend to discover widely different mechanisms of thought as lying at the root of the neurosis. The universality of the sexual basis so vehemently asserted by partisans is strenuously denied by other investigators, who them-

selves propound mechanisms that are not admitted universally. On any theory all these observers cannot be right, and in physical science, if we found that honest experimenters obtained consistently different results with a certain method we should not hesitate to impugn the validity of the method. A form of inquiry which involves the exclusive concentration of the mental activity of the subject on the performance of a task set to him by the observer renders him particularly sensitive to any form of stimulus that he may receive from the observer. We have seen in the preceding lectures that the expression of mental activity is far from confined to vocalisation. Movements of every variety are involved; the more obvious movements to an observer have in point of fact not been dwelt upon, that is, such movements as are evidenced by facial expression, eye movements, and the play of the pupils, for the sole reason that though obvious to the eye they present overwhelming difficulties to instrumental registration. An example from the animal world may illustrate the part that such movements play in communicating our approval or disapproval.

THE THINKING HORSES OF EBERFELD.

I know of no better example of the perils that beset this form of investigation than the story of the "thinking horses" of Eberfeld. A Prussian school-master, Herr Krall, succeeded in educating horses so that they would indicate the sum or product of numbers written on the blackboard by stamping the hoof the proper number of times. Later on they acquired the power of doing divisions and extracting cube roots. They were investigated by most of the eminent psychologists of Germany and many were the papers written about their feats. The bona-fides of their master were undoubted and they would perform equally well in his absence. As time went on these animals developed superhuman powers: they would not only solve the difficult problems of the blackboard, but they would guess correctly and stamp out the number of which the observer was thinking. At this stage they were investigated by Stumpf; he confirmed their marvellous powers of guessing the numbers thought of, and then proceeded to test their ability when blindfolded. The horse did everything it could to see the observer from under the bandage; when it succeeded in doing so the answer was right, but when the blindfold was effective it was generally wrong. That solved the mystery; Stumpf found that, in common with every observer, when the number that he had thought of was stamped out he made a little involuntary gesture of assent which the quick eyes of the horse noted. I have often repeated the same experiment, taking the part of the horse myself, and so long as the subject is innocent of the method employed I have seldom failed. To an experimenter conducting an analytic examination no stimulus word can be totally without affective import, be it the expectancy of a result or the recognition of its utility.

RESPONSIVENESS OF THE SUBJECT OF INQUIRY.

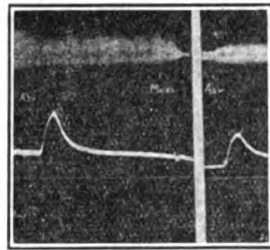
The subject is dissociated from all other stimuli than those communicated by the observer. He is warned to respond without self-criticism or hesitation. If with a casual fixation of attention it is easy to repeat the experiment of the Eberfeld horse under the conditions of a psycho-analytical investigation there must be many signs such as the inflexions of the voice and the play of the features, that it is impossible to control. In such a responsive attitude on the part of the subject wilful deception of course plays no part. Evidence of the extent to which the responsiveness of the subject can be raised under appropriate conditions can be found in the Proceedings of the Society for Psychical Research. Whatever be the eschatological value of these documents they certainly contain a mine of information to the student of abnormal psychology. The alertness with which almost imperceptible hints are adopted, the amazing accuracy with which the observer's mind is interpreted by perfectly honest subjects who have placed themselves as purely receptive instruments in the hands of the observer whilst under the belief that they are giving utterance to the thoughts possessing their brain, must give pause to anyone who notes the conditions under which analysis is carried on. Even when suggestion is discounted it is impossible to ignore the part played by the analyst in the interpretation of the results. I have sufficiently dealt in a previous lecture with the incommunicable uniqueness of states of feeling. It is for these and similar reasons that, in so far as it has appeared to be desirable to inquire into the associations connected with any particular phase of conduct, I have confined myself to a very superficial examination that readily permits of an objective control. The patient is allowed to tell his history without interruption or question whilst a continuous record of his skin resistance to a constant current is photographically recorded on a roll of bromide paper. The observer sits behind him, and the main headings of his discourse are taken down on a sheet of paper ruled so as to allow the time at which any statement was made to be compared with the timed record of his resistance. I have made many such records and they form curious psychological documents.

INCONSTANT REACTION OF THE VEGETATIVE SYSTEM.

It is by no means those statements to which the patient appears to attach most importance that furnish evidence of an affective response; obvious attempts to achieve pathos may leave the galvanometer unmoved, whilst the narration of some less prominent incidents which reveal the general orientation of the patient's attitude will evoke a well-marked galvanic reflex. Even with such precautions the results obtained must be interpreted with considerable caution. Sherrington and Grünbaum have shown that stimulation of a cortical area after an interval by no means invariably evokes the same form of response, and we may interpret this as a physiological

demonstration of the fact that our reaction at any given time to a stimulus is determined to a great extent as to its form by the particular equilibrium in which the stimulus finds the nervous system. Still more so is this true of the mechanism of the affective response. The vegetative nervous system does not always react in the same fashion to the same type and intensity of stimulus. I was able in conjunction with Symes to furnish an experimental demonstration of this fact in connexion with the sympathetic innervation of the bronchial muscles. When the neuro-muscular junction of the sympathetic nerve-supply to the bronchiolar muscles is stimulated by the same dose of adrenalin a precisely opposite type of response may be elicited, according to the condition in which the stimulus finds the bronchiolar mechanism. If the bronchioles be

FIG. 3.



Antagonistic action of adrenalin on bronchioles. Firstly, when dilated; secondly, when constricted.

constricted the stimulus will cause dilation; on the contrary, when the bronchioles are dilated sympathetic stimulation will cause constriction (Fig. 3). A very little observation of our own feelings reveals a similar process. A stimulus that has evoked a pleasurable feeling may on repetition prove disagreeable, and vice versa: "Nessun maggior dolore che ricordasi dei tempi felici nella miseria." It by no means follows that a stimulus evoking a galvanic response indicating

its "nocuous" nature always did so. As a method of therapeutics the attempt to disintegrate the aberrant mechanism by the introduction of fresh associations, if the contention as to the organic disturbance underlying the neuroses be correct, can only claim to be a form of symptomatic treatment. In the absence of efficient radical treatment symptomatic treatment is justified, so long as it is not mistaken for a process of radical cure. It is as symptomatic treatment that the methods of psychotherapy must justify themselves, and there can be no greater disservice rendered to its claims than the talk of "cures" evidenced by the sublimation or removal of certain symptoms of a particular neurosis.

HYSTERIA.

So far I have dealt with the fundamental characters of neurosis in which the physical disturbance is manifested by a hyperactivity of the mechanism of affection. I will now turn to a type of neurosis in which I have reason to think that the fundamental disorder is an impairment of the activity of the mechanism of affection; the forms of neurosis that fall under this definition are those designated as hysterical or pithiatic. The conception of the nature

of hysteria has undergone a radical change in recent years. The supposed stigmata that seemed to constitute the neurosis an organic disease have been discarded one by one. Under the ægis of Babinski we have learnt to eliminate all symptoms from the clinical picture of the neurosis that are not entirely under the control of the will, until we have reached a point when our knowledge of hysteria may be summed up in Babinski's famous dictum—"Entre l'hystérie et la fraude il n'y a qu'une différence d'ordre morale." Hysteria, then, can only be distinguished from conscious simulation by a purely subjective criterion; it may appear to be a retrograde step to return to the old search for organic disturbance after our symptomatology has been carefully purged of the so-called stigmata, which have one after another been shown to be simply the response of the patient to auto- and hetero-suggestion. If, however, the view that a neurosis is the expression of an organic disturbance is to be consistently maintained, an attempt to demonstrate the existence of signs of such disturbance in hysteria is a logical necessity. The implications of the view propounded by Babinski do not seem to have been clearly recognised. Starting with a purely objective analysis of conduct, he finishes by abandoning all attempts at an explanation in terms of neuropathology and refers us to a purely subjective standpoint. Any attempt to understand hysteria must be founded on some knowledge of the general orientation of the behaviour of the hysteric before his conduct brings him into contact with the physician. Such knowledge is rarely directly available to the specialist; it may more often be gleaned from information supplied by the family doctor or by intelligent relatives. The picture obtained from these sources is that of an egocentric individual without strong or durable emotions, though very anxious to impress the outer world with the gravity and intensity of his experiences. Always more ready than a well-bred person should be to impress his fellows, he will not willingly apply himself to any task involving strenuous exertion, fatigue, or danger. The total personality conveys an impression of flimsiness. He appears to be a very different person to the volcano of ill-suppressed sexual passions that some writers on psychotherapy have portrayed. The symptoms of hysteria convey to the observer a certain general impression of what can be called theatricality—though possibly the stage ill deserves such a comparison. The necessity under which the cinematograph actor finds himself of conveying his mental states to the audience by emphasising all the mechanisms of expression has much in common with the conduct of the hysteric. Such vague impressions might lead us to look for indications of enfeeblement of the mechanism of affection which reinforces and protects the general tendencies of normal conduct. In 1918 I had the opportunity of examining all the cases of neurosis that passed through the Maudsley Neurological Clearing Hospital, which at that time had over six hundred beds. I found that the large class of patients exhibiting those motor and physical symptoms which

constitute the hysterical syndrome could be readily differentiated from other types of neurosis by the extraordinary depression of the galvanic response to any form of stimulus. Such patients would start or tremble at a loud noise or painful stimulus, when a normal man would hardly budge, but the galvanic response would be either absent or less than normal. Though they might talk of great emotional perturbation there was no corresponding galvanic reflex. The *mise en scène* of the galvanometer room seemed to be extremely conducive to the exhibition of hysterical crises, and I had the opportunity of observing the galvanic reflex during many such scenes. One young soldier suffering from a hysterical contracture of the foot broke down during an examination; tears rolled down his cheeks, he addressed his dead brother in language savouring of a South London melodrama, he asked why he himself had not been killed in his brother's place so that the favourite son might have been left to comfort his poor old father, and all the time whilst he wailed and wept the spot of light from the galvanometer mirror remained steady. In my second lecture I pointed out that in the recitation of dramatic poetry the counterfeiting of rage or grief, no matter how dramatically performed, is unaccompanied by the electrical signs of activity of the affective mechanism. In these observations we have, I think, the key to hysterical behaviour. It is purely imitative. I published these results in a very condensed form at the meeting of the British Medical Association in the autumn of 1918, and since then have seen no reason to modify the conclusions that I then formulated. I not only found that the response to the alleged emotional states is absent but that the hysteric reacts subnormally to all forms of adequate, that is nocuous, stimuli. We are therefore entitled to assume that the activity of his mechanism of affection is subnormal. In the second lecture I demonstrated that a study of the time relations of the galvanic and other forms of response to nocuous stimuli shows that the stimulus is recognised and elicits an appropriate cerebral response an appreciable time before the bodily mechanism of affection reacts. We have, in fact, a kind of dualism—on the one hand the discriminatory mechanism associated with intelligent behaviour, and on the other the reaction of the organism as a whole to a nocuous stimulus. Herein lies the explanation of hysterical conduct. The hysteric is as capable as a normal man of recognising that the situation in which he finds himself is one of potential peril or discomfort, he can respond immediately to the situation by an appropriate cortical reaction; but if the stimulus be continued his activity lacks the reinforcement supplied by bodily reaction. To determine his line of conduct a representation of the situation is necessary, and such a representation must normally involve the activity of the mechanism of affection, since in no other way can the unpleasantness of the situation which reinforces the intellectual appreciation of its danger be recognised. Deprived of this determining force his reaction to the situation will be at the mercy of any casual stimulus. We have had objective evidence that the affective reaction fails

him ; he has then recourse to other forms of expression more or less distantly associated with the feeling of unpleasantness. The association of bodily ailments with the feeling of distress will most readily furnish the mechanism by which the patient endeavours to represent to himself and to symbolise to the external world the fact that his activities are impeded or threatened by some nocuous influence in the environment. Hence the hysterical symptoms really constitute a method of expression primarily for egoistic and secondarily for social needs which has been conditioned by an organic disability of the mechanism of affection. Another cardinal symptom of the hysteric is referable to the same organic disability. All writers on hysteria have emphasised the abnormal suggestibility of the hysterical subject. Suggestibility has been defined by McDougall as a process of communication resulting in the acceptance with conviction of the communicated proposition in the absence of logically adequate grounds for its acceptance.

The destructive criticism of logic by the pragmatists has taught us one thing—that is, that no judgment is without its affective side, a truth which, though by no means new, since it is implicit in the revolt against formal logic which began in the psychological studies of Fries and Herbart, is still occasionally forgotten. Our strongest bond with reality is that of the feelings which constitute our strongest defence against the irrational. Mind dissociated from feeling is mind very much at the mercy of any suggestion. It is the bodily reaction against a suggestion that is in discord with the general tendencies of our activity that is the real guarantee against its acceptance. It is just this defence that the hysteric lacks ; to a greater or less extent his activities can be unduly influenced both by autogenous and heterogeneous suggestions. In other words, the innate and habitual pattern reflexes, having lost the mechanism of bodily reaction by which they reply to stimuli tending to interfere with their activities, are no longer the potent protective system that they constitute for the normal man and can be displaced or dissociated by any new stimulus of sufficient potency. Great as has been the work of Babinski and his school in demonstrating the mimetic nature of hysterical symptoms, it has been needlessly impaired by the criterion that they have adopted of what constitutes a hysterical symptom. Limited by the subjectivism that defines hysteria as only differing from fraud in its moral aspect, they decline to consider as hysterical any symptom that cannot be produced by an effort of will. This is a return to the subjective method par excellence. Of will and its limitations we have no objective knowledge, and as Spinoza once said : “ No one has yet learned from experience what the body regarded merely as a body is able to do in accordance with its own natural laws, or what it cannot do. For no one knows enough about the constitution of the body to examine all its functions.”

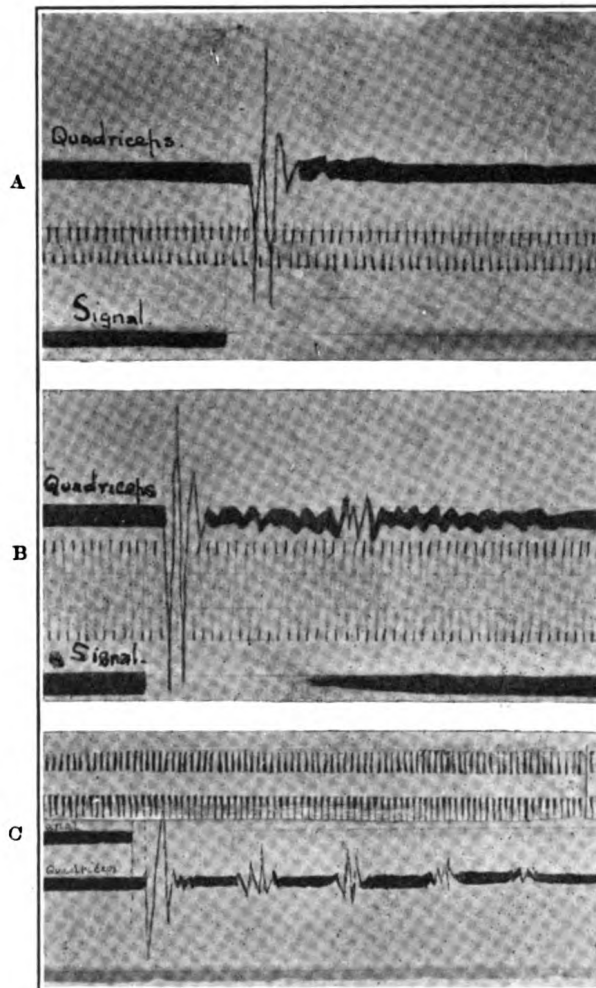
The study that we have just made of the movements manifested during cerebral activity has revealed a

series of motor, circulatory, and glandular reactions, which, though not capable of being directly influenced by volition, are in their totality the expressions of volitional effort. Owing to his dissociation from states of feeling the hysteric appears to readily assume that state of muscular hypertonicity which we have observed as an accompaniment of concentrated effort, and the reflex response to certain stimuli is in consequence greatly exalted. The response to auditory stimuli frequently takes the form of an exaggeration of the normal "start." I have pointed out that the latent period of the start in man is extremely short, not much longer than the 0.05 second found by Sherrington in the decerebrate animal and the exaggerated start of the hysteric, having the same latent period as that of a normal man, a voluntary origin must therefore be ruled out. Even more striking is the exaggeration of the knee-jerks. The response may not only be increased but followed by a series of irregular clonic contractions—which may, however, be readily differentiated from the true quadriceps clonus of a lesion of the pyramidal tract when recorded by the oscillograph or the string galvanometer (Figs. 4). As Wertheim Salomonson has pointed out, the electromyogram of the true clonus points to an origin different from that of the spurious hysterical clonus. None of these phenomena are directly referable to voluntary activity, but they are consistent with the supposition that the patient is in the same state of muscular hypertension as a normal person whose whole organism is concentrated on a particular voluntary effort. I have occasionally succeeded in obtaining myograms exhibiting a similar functional clonus from normal subjects concentrating all their attention on squeezing the dynamometer. It is generally accepted that when a case of hysteria is characterised by some paralytic or motor symptom which simulates the effects of a definite organic disturbance it is always possible to differentiate between the hysterical symptom and the organic one by the fact that such subsidiary mechanisms as would be certainly affected in organic lesions are not affected in the case of hysteria. In hysteria, owing to the ignorance of the subject of the physiology of the symptom mimicked, the affection of these subsidiary mechanisms would never be suggested to him.

Whilst in the great majority of cases this rule holds good, and is indeed sufficiently constant to be our standard method of differentiation between organic and functional disease, it is not quite universally true. It would appear that certain mechanisms are so closely allied with the normal exercise of particular functions that although their existence and connexions are unsuspected by the patient it is impossible for the main function to be suspended without their being also affected. Hurst has pointed out that in cases of total hysterical deafness the start or jump to a loud sound may be suppressed. Such suppression of an involuntary mechanism does not, however, appear to be true of the affective reactions. I have never failed to obtain a galvanic reflex to

a loud sound in cases of hysterical deafness. Another example of the difficulty in drawing an absolute line between voluntary and involuntary symptoms in hysteria is furnished by the vestibular reactions.

FIG. 4.



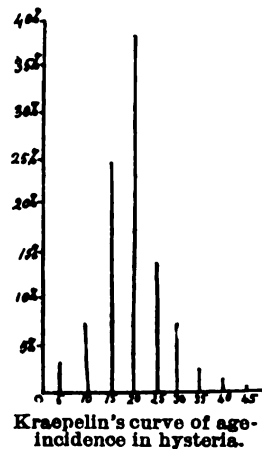
Electromyograms taken with Bock-Thoma oscillograph.

- A, Normal knee-jerk. B, Hysterical knee-jerk, with functional patellar clonus. C, Knee-jerk, with patellar clonus in spastic paraplegia.

I have been able successfully to suggest a definite vertigo to two cases of hysteria who complained of ill-defined symptoms of giddiness. In both these cases when they were asked to perform the pointing

test with their eyes shut they invariably showed a deviation corresponding to the direction of the suggested vertigo. Thus in the absence of the start reaction we have an involuntary mechanism definitely suppressed and in the vertigo reaction we have it appropriately altered, when a strict interpretation of hysteria in the terms of Babinski's definition would require them to remain unaffected. What may be the nature of the pathological changes responsible for this hypoexcitability of the mechanism of affection in hysteria it is impossible at present to specify. That the organic change exists prior to the development of the more obvious symptoms may be inferred from a study of the previous history of such cases. The diagram (Fig. 5) is constructed from the statistics

FIG. 5.



Kraepelin's curve of age-incidence in hysteria.

of Kraepelin of the age-incidence of hysteria based on 430 cases. Although the years immediately succeeding puberty are those most affected by "Sturm und Drang" it would hardly be expected that the fall in the curve would be so steep were it not that a definite amelioration of the organic response rather than a disappearance of environmental stress is the responsible factor.

CONCLUSION.

At the risk of wearying by reiteration, I will again call your attention to the absence of any proof that the early experiences of the hysteric differ from those of the majority of mankind and to the fact that they therefore cannot be held to play any considerable part as predisposing factors. Of the disturbances of mechanism responsible for the psychoses I do not propose to speak. We have already seen how the observations of Mott and his pupils may be considered to have definitely settled the question of the organic origin of dementia præcox. The profound metabolic disturbances in manic depressive insanity, though still awaiting investigation, are indicative of a similar organic basis. Through the kindness of Dr. Mapother I was able to satisfy myself that the seemingly violent emotional activity of mania is unaccompanied by objective signs of hyperexcitability of the mechanism of affection. Were but a tithe of the attention at present devoted to the classification and tracing of psychogenic disturbances in the insane given to an objective study of their nervous mechanism by physiological methods, we should probably before long have remedied the deplorable condition of the pathology of insanity. Unhappily asylum authorities have not yet recognised the necessity for observers skilled in physiological methods.

In concluding these lectures I must acknowledge with the profoundest sense of obligation the kindness and encouragement in their preparation that I have received from Sir Frederick Mott, in whose laboratory at the Maudsley Hospital the experimental work connected with them has been performed.

I also wish to acknowledge the assistance received from the Board of Control in the purchase of some of the apparatus used for the experiments conducted in connection with these lectures and for a grant enabling me to re-publish the same from THE LANCET in the 8th Volume of the Archives of Neurology and Pyschiatry from the Pathological Laboratory of the Maudsley Hospital.

Lectures
ON
MENTAL DEFECT AND CRIMINAL CONDUCT.

*Delivered to the Members of the Class of Psychological
Medicine, Maudsley Hospital,*

BY SIR BRYAN DONKIN, M.D., F.R.C.P.,

LATE ONE OF H.M. COMMISSIONERS OF PRISONS.

LECTURE I.—ON "MENTAL DEFECT": ITS GENERAL
AND SPECIAL IMPLICATIONS.

(Delivered on Oct. 25th, 1920.)

THE presence in a notable number of offenders against the criminal law of clear evidence of mental defect, which *practically* marks them off from the bulk of the law-abiding community and from the majority of criminals as well, is recognised by all those who have good opportunities of observing and conversing with convicted prisoners. I lay purposeful stress here on the word "practically," using it without making any assumption that this particular group of criminals is otherwise differentiated. I mean only that such criminals are the subjects of patent mental defect of some kind or other, which is recognisable, with but little expert knowledge, from the quality of their conduct, and quite apart from any consideration of the crimes for which they have been convicted or of the probable nature and origin of the mental defect inferred. Such criminals as these have been for a long time regarded by the English prison authorities, for the purpose of special treatment, as being practically a class apart from the average prisoner, and have been described in the *convict* prisons, the inmates of which are all sentenced to penal servitude (i.e., for three years or more) as "weak-minded" and more or less irresponsible for their misdoings. They were thus recognised in the several convict prisons for a considerable period of time before I became a Commissioner of Prisons 22 years ago. All of such weak-minded convicts have now for many years been congregated in one only of the convict prisons, where they have appropriate work, under special regulations, and are mainly regarded and treated as hospital cases under the immediate supervision of the medical officers. Several of them are ultimately certified under the lunacy law and sent to asylums, and others are dealt with under the recent Mental Deficiency Act.

A general recognition of this kind of criminal has

existed in this and other countries for a long time, as is manifested in a still growing mass of literature dating from about half a century ago, and devoted more particularly to the study of criminals themselves than to that of crime and the problems of punishment, which had mainly absorbed the attention of prominent writers on penology during the eighteenth century and most of the nineteenth. It is only in comparatively recent times that the study of criminals has to some extent taken the place of that of penal jurisprudence, and that the conception of what is called a science of "criminology" has made its appearance.

MENTAL DEFECT AS A FACTOR IN CRIMINAL ACTION.

I cannot attempt to give in these lectures even a short compendious account of the large number of modern works, mostly of non-English origin, on this subject, but must confine my attention only to such topics as may be necessary for the elucidation of my purpose. This purpose is, chiefly, to state as clearly as I can my views on the extent of the rôle played by mental defect as a factor in criminal action, and, incidentally, to glance very briefly at the relation of that rôle to the penal treatment of offenders. And I may say at the outset that after considerable practical experience and reflection, and no little study of British, American, and European writings on the subject, I am forced to the opinion that no "science" or systematic study of criminals in the mass, sufficiently definite to be of great practical value, is likely to be arrived at. I have long been convinced, in common with other observers of our species, that all human beings are potential criminals; and that a large number of men and women commit crime, in the sense of wilfully injuring society for their own individual purpose, whether or not they are detected in breaking, or even break, any existing law. The study of criminals is, indeed, an integral part of the study of man, and of human psychology especially; but the indefinite nature of the differences that have as yet been established between criminals and law-abiding men in the mass seems to me to point away from the prospect of establishing anything like a special and clear-cut body of knowledge which would merit the name of a "science" of criminology. I trust that my subsequent remarks will justify this initial expression of opinion.

I have used in my opening sentence the term "mental defect" in its widest sense, not in the more special sense as it occurs in the Mental Deficiency Act of 1913, and as I shall usually employ it later in these lectures. For the moment I mean this term to cover all such cases, whether described as "unsoundness" or disorder, or defect, of mind, as are recognised by the Lunacy and Mental Deficiency Acts, as well as such other cases as may need special care and control, but cannot be included under any category which is held to qualify them for technical certification. It is clear that all the cases recognisable under these Acts—i.e., persons of unsound mind, idiots, and the other groups specified in the Mental Deficiency Act—are cases of

defective or disordered mind; although, equally of course, not all cases of defective or disordered mind are recognisable by either of these Acts.

I would, therefore, recast my opening sentence thus : There is a notable number of law-breakers of all kinds, not only of those sentenced to terms of penal servitude, but also of those convicted for lesser offences against the law, who are quite clearly the subjects of mental defect in some of its recognised forms and degrees. It is, moreover, largely but not by any means wholly with respect to this class of offenders that the important questions of their responsibility, or degree of liability to punishment, and of their appropriate treatment, are concerned.

With regard to the prevalence of certifiable insanity in prisoners, compared to that in the population at large, as computed from the annual returns of asylum inmates, and of prisoners detected as insane and certified as such after coming to prison, this is practically the same; but, as it is stated in the late Dr. Charles Goring's well-known work on "The English Convict," if the number of *deaths* of prisoners certified insane and subsequently removed to asylums are added to the prison returns, "a high degree of association between crime and insanity is manifest." This is a valuable corroboration of the impression received in prisons generally of the not inconsiderable numbers who come into prison with signs of easily recognisable insanity, and who are promptly certified and, being sent to asylums, are no longer returned as prisoners. It has, indeed, been long known that insanity of an unquestionable kind is a very frequent contributor, if not practically the chief factor, in the production of many crimes, homicidal or other, characterised mainly by injury to person or property, and also including some "political" crimes perpetrated on the strength of unquestionably genuine delusions.

When I arrive at the closer consideration of the relationship between mental defect and criminal action generally, which will be the subject of my next lecture, I shall have to limit my remarks almost entirely to mental defectives other than "insane persons" or "lunatics" technically so-called, whether or not such mental defectives be actually certifiable under the recent Mental Deficiency Act of 1913. For it is notably in connexion with this class of cases that the scientific and practical aspects of the subject in hand becomes of high importance and has been the subject of much discussion. It is here that we encounter the chief question proper to our theme—viz., whether the mass or the majority of law-breakers are signalised by such marks of mental defect as to justify their being regarded from a scientific point of view as almost wholly the product of "natural" or "constitutional" defects, and but slightly, if at all, of the "force of circumstances" that have acted upon the individual law-breakers through their lives. But before I enter upon this main question I must mention a few initial difficulties which beset more or less the study and exposition of "mental defect" in its more special sense, without giving regard for the moment to its relation to crime. Some of these difficulties are of a practical, others of a theoretic, nature.

THE MEANING OF THE TERM "MENTAL DEFECT."

The first point for note is the content of the term "mental defect" in general, and as it is interpreted in the Act of 1913. In *general* the study of mental defect is a matter of psychology, and in common with that of mental soundness the term connotes a meaning which must vary according to views held by the student touching the nature of mind and its relation to the bodily organs, and especially to the brain. We are all aware that these views are numerous, and are held with considerable tenacity by their various adherents. They may be roughly divided into opposite groups, commonly known as the "scientific" and the "metaphysical," and by many other pairs of opposite terms: such as "materialistic-idealistic" or "mechanist-vitalist."

The unnecessary introduction of the fundamental problems of psychology into some questions of practical import in the study of mental faculties is not infrequent, and usually tends to produce confusion. It has often struck me that these problems have been inserted or have crept irrelevantly from time to time into inquiries held concerning the recognition and care of persons who are "mentally defective." As I was about to write this part of my lecture, and thinking of a short form in which I could express the ground on which most of the disputants I allude to could meet in peace, I came upon the deeply interesting address delivered last July by Sir Frederick Mott to the Congress of the Royal Sanitary Institute and found just what I wanted, at the beginning of that part of his address which dealt with "objective psychology."

"The furniture of the mind is the memory of the experiences of our life and the bonds that unite them; there can be no mind without memory and no memory without body. The furniture of the mind of primitive man" (which is what we study as mental qualities) "consists largely of the memory of experiences connected with the primal instinctive activities of nutrition by capture of food, of self-preservation, and avoidance of pain, of reproduction, and of the 'instinct of the herd' (or, as some would put it, of imitation). The civilised man is able, not only to store up and utilise his own experiences, but by means of language and abstract thought to associate these experiences with those of innumerable other human beings who live and have lived, and thereby to reason on a much higher plane, and utilise his psychic (or mental) energy in a multitude of refined ways for the ultimate ends of the primal instincts."

Whether we are all agreed or not to look upon the word "mind" as the name given to the sum of the items of furniture of the primitive mind thus set forth in brief by Sir Frederick Mott I think that most *will* agree that for most useful purposes we shall not quarrel about accepting the mental content which he signifies as sufficient to denote the essence of what we all mean in speaking of "mental phenomena," mental soundness, and mental defect. We can all find here, without philosophising more deeply, a sufficiently satisfactory basis for such a common conception of the general meaning of those psychological terms the use of which is unavoidable.

As regards the *special* meaning of the term "mental defect" as employed in the Act of 1913 it must be remembered that the Act technically recognises for the first time a large class of persons of all ages who were not held to be certifiable under previous Acts, but who, according to a mass of evidence produced by the Royal Commission's report which was the immediate occasion of the passing of the Act, needed legal control of some kind. It was at the instance of some experts in the study of the human mind, and, more especially, of certain public bodies of active social workers, that the Government in power in the first quinquennium of this century felt it right, after taking counsel from various sources, including the Prison Commissioners, to appoint a Commission to inquire into the alleged necessity of fresh legislation in the matter of the "feeble-minded." The chief finding of the above-named public bodies at first, and subsequently of the Royal Commission after much inquiry, was that by far the largest number of these uncertified or uncertifiable persons were those generally known, in this country especially, as "feeble-minded." Possessing superior mental activities to those of persons known as "imbeciles" or "idiots," these feeble-minded, in virtue of this very superiority, were mostly left without care or control, although they were capable of causing a grave amount of social harm in many directions, and were unable to contribute to their own living without supervision. In America and elsewhere this large group of persons had been similarly recognised by experts and described as the highest grade of "imbeciles," or mental defectives not certified as insane. But the term "feeble-minded" was then in general use in America as including also "imbeciles," and even "idiots" of the lowest grade. At the present time, however, the term "moron" (a Greek neuter adjective, meaning "foolish") is now applied by many American writers to this high grade group which is called "feeble-minded" in the English Mental Deficiency Act. Yet it seems that the American and English terms "moron" and feeble-minded are not quite co-extensive in their denotation, for the former is more limited than the latter to cases evincing defect of the mental faculty of intelligence alone; and thus, apparently, less regard is paid to those persons who, with slight, or as some say, *no* remarkable defect of intelligence, show such constant and patent defects of conduct, (indicating disorder in the sphere of emotions, or of morals,) as render them dangerous members of society.

PRACTICAL DIFFICULTIES IN DEFINITION.

But what especially concerns us here, from the practical point of view, is that the Mental Deficiency Act requires a certain definition of "mental defect" to be attested in the certificate; whereas the Lunacy Act contains no definition of the terms "unsound mind" or "idiot" which denote the only classes of persons who can be certified under it. In the Lunacy Act there is no definition at all of Lunacy as a state or *condition*. Only in the Glossary to the Act it is said that "lunatic"

—i.e., the word in the Act—means a “person of unsound mind or an idiot.” It can scarcely be doubted, however, that some practical distinction was obscurely hinted at in this glossarial interpretation; it seems to indicate that the person of unsound mind had once been of a sound mind, and that the idiot was born an idiot; and thus to bring in the very old and somewhat practical division into two classes of people not “right in their minds.” In more recent days a similar distinction is frequently made by the use of the somewhat loose or inaccurate terms of “acquired” and “congenital.”

But although “idiots” can be certified under either the Lunacy or Mental Deficiency Act indifferently—this being a further instance of the regrettable separation of the two Acts—the higher-grade cases of mental defect, at least in *England*, cannot be certified under the Lunacy Act. I have been told by some, however, that the Scottish law is interpreted more elastically in this respect. The fact remains as a cause of difficulty and confusion that the lunacy certificate is, in form, mainly a statement of observed facts of conduct: whereas the mental deficiency certificate may be, and is often, taken as directing the certifier to testify that the condition of mind in question actually existed from birth or an early age; and this interpretation implies that this Act takes some cognizance of the further question of the origin or cause of the defect, which question is not raised or implied in the lunacy certificate.

I did not at first regard this last-mentioned imperfection of the Mental Deficiency Act as likely to cause very great difficulty, provided an intelligent and liberal interpretation of it were encouraged, though I detected the flaw when I saw the Act in its later form on its appearance in 1913. But I have in subsequent years been convinced, by communication with some of the best experts whose duty it has been to certify under this Act, that the form of the certificate is a stumbling-block to many. I am of strong opinion that the mere *descriptions* of the various grades of mental defect which the Act is concerned with should never have been converted into a statutory *definition* or incorporated in the required certificate. This change was introduced first in the drafting of the Mental Deficiency Act of 1913, which followed on the Bill withdrawn from the House by the Secretary of State owing to opposition in the preceding year. I have previously dwelt at some length on this point in various papers published in the *Journal of Mental Science*, and also at several conferences concerning the diagnosis and treatment of the feeble-minded, and need say but little further on it now. There seems to be some reason to believe that this difficulty is becoming more or less recognised officially, and that in certifying cases of “mental deficiency” a clear statement of opinion, based on reasons clearly set forth, that the instance in question belongs to the category specified in the Act, is usually accepted as sufficient for the validity of the certificate. It is certainly true that the form of the lunacy certificate seems at first sight simpler, and thus the easier of execution, in order to meet the requirements of the Act; but it is also true that the lunacy certificate may not seldom present difficulties equal to those of the Mental

Deficiency Act. The essence of the certificate in both cases must consist in reasoned opinion. In connexion with our present subject this difficulty of certification is mostly met with in the case of adult criminal defectives, whom it is desirous to certify for the purpose of placing them under more appropriate care and control than that of the prison regime. For in many instances it is impracticable to ascertain the facts of the early history of criminals, even of the sane.

THE CLASSIFICATION OF SOCIAL INEFFICIENTS.

The second point I have to note is this. Some writers have held that the recognition of "mental deficiency" according to the Act depends on the observation of defect of intelligence alone, but that such mental defectives do not form the whole of the subjects whom the Act is intended to control. Opinions, moreover, differ as to whether in the assessment of "mental deficiency" in any case, criminal or not, account should be taken of peculiarities of mental manifestations other than those clearly occurring in the sphere of intelligence, and this consideration is apt to lead to much controversy and confusion.

However, as far as the criticism of the Act itself is concerned, this much may be said on both of these objections: (1) There is no limitation in the Act of the meaning of the term "mental" to the sphere of thinking or intelligence alone—such limitation, that is to say, as would exclude regard of disorder or defect referable to the sphere of the emotions; and (2) the general test of mental condition by careful observation of conduct is practically set forth in the description given in the Act of the various groups of persons intended to be dealt with. This is also true in cases of certification under the Lunacy Act, in which it is not seldom very difficult or impossible to demonstrate any disorder in the sphere of thinking, and yet to find no practical hindrance to the diagnosis of "unsound mind."

It is illogical and erroneous to assume that the term "mental defect" does not cover defect of mind generally (as displayed in the various manifestations which most psychologists recognise as signs of mental action), and then to proceed to infer that there are large numbers of persons liable to be dealt with by the Act who are not mental defectives, but rather "social inefficients," on the ground that their grade of intelligence is not lower than that of average persons. Stress has been laid on this special interpretation of mental defect by those who hold that the constitutional or natural factors of the various mental characters of men can be disentangled from those which are adventitious or due to the external influences of each individual's experience and circumstances; and that then, being thus disentangled, the faculty of intelligence can be dealt with as a simple character not subject to further analysis. I shall have to deal with this point again later in reference to its bearing on the relation of mental defect to crime. It is enough to say now, in connexion with the criticisms I have mentioned, that there are many observers of mentally

defective persons who hold strongly that even in the case of those numerous "social inefficients" who do not display at first sight any lack of intelligence evidence of some such lack can always be elicited; and, further, that few, if any, psychologists, however widely they may differ on many important points, confine their conception of "mind" to the faculty of intelligence alone. The time is now past when a definite "delusion" was required to be established for the validity of a lunacy certificate.

HEREDITY OR ENVIRONMENT.

My third and last preliminary note touches on some difficulties in connexion with the Mental Deficiency Act which have been caused by the introduction, not easily avoided, of biological questions on the origin of mental defect. This leads to discussions regarding heredity between those who hold widely different views as to the meaning of the word "heredity," and especially between those who, on the one hand, regard all mental characters that lend themselves to study as referable in origin *either* to natural transmission, *or* to acquirement derived from external influences, and those who, on the other hand, regard such mental characters as necessarily requiring both these elements. In the next lecture, when dealing especially with the criminal aspect of our subject, I shall refer again shortly to the eminent importance of the part played by external influences, or "environment," or "nurture" on the highly complicated nervous structures of man on which depend the various manifestations or functions which we call "mind." But here I wish to lay stress only on what may be called the "natural" or inborn element which in many patent cases of so-called "mental defect" is the immensely predominant factor. Experience makes specially evident the tendency of this class of cases to "run in families," and, in many of them, to be recognisable in very early life, even without showing any signs of significant physical defect. I do not imply, in saying this, that this class of very salient instances of mental defect are, psychologically or otherwise, distinguished in any hard-and-fast way from the minor specimens of mental defect of various grades which are less obvious to observation and thus do not attract general attention. The omnipresence of an inborn and transmissible element in the development of all mental characters whatever, whether in their healthy or pathological aspects, is not doubted by any scientific student of psychology, and need not be regarded as a matter for argument.

At present we have little definite knowledge of the cerebral and other organic conditions which necessarily underlie actual mental manifestations of all kinds and grades, average, excessive, or defective, common or rare, as the case may be; and we are forced to rely mainly on the careful clinical observation of individual cases for indications of such mental defect as seem to render it desirable or necessary that the subject of it should be specially treated. It may yet come within our knowledge that there is a definite association of

some special brain or other organic conditions with certain differences of mental potentialities. Or further comparative study of the brains of human mental defectives and anthropoids may possibly throw more light than we have now on the question whether in some cases clearly manifest degrees of early deficiency may be truly reversional in character. But such knowledge, if gained, would not help us much towards making an accurate diagnosis of degrees of mental defect or disorder during the life of the subjects of it. In practice, however, as I have said, degrees of defect indicating certain lines of action in cases which come under question may generally be discovered by careful study of the *individual's* conduct and of his capacity to learn what is fundamentally requisite for a human being to know in order to live sanely and more or less successfully with his fellows. And this can be achieved without necessary reference to any strictly rigid standard of mental capacity. I cannot enter here into the highly interesting question of the various tests which have been proposed for ascertaining, by comparison with a standard based on the average intellectual capacity of growing children, the capacity of apparently defective persons of any age; but I may say, only by the way, and judging from the information I have gathered from others, and from reading, rather than from my own experience, that short of being regarded as providing any royal road to certification under the Act, or as an *authoritative basis* for evidence given in a court of law, such tests are likely to prove of considerable use in recording cases with a view to making reports for the preliminary grading of children in classes or for serving as a help to observers towards recalling results of the successive interviews which are mostly necessary in arriving at any practical decision.

LECTURE II.—ON THE RELATION OF MENTAL DEFECT TO CRIME.

(Delivered on Nov. 1st, 1920.)

I reviewed in the last lecture the matter of mental defect generally, as far as seemed necessary before considering my main subject; and then commented on some of the difficulties that are met with in dealing with mentally defective prisoners from the point of view of their description, care, and control. I begin this lecture with a few explanatory words on what I mean by crime, as introductory to the subject of its relation with mental defect. There is a legal, and also a psychological—moral, and more or less popular—meaning of the term “crime”; and these two meanings frequently tend to become mixed in writing and in thinking. In the legal sense crime means offence against certain existing laws, and “criminal responsibility” thus means liability to punishment under those laws. In the wider sense crime implies conduct injurious to society, and, as Dr. Mercier has said in his recent book on “Crime and Criminals,” “by this must be understood the society to which the criminal belongs.” Thus the more comprehen-

sive concept of a "criminal" is that of a person who acts wilfully in a manner which is injurious to society, one in whom self-regarding conduct is frequently preponderant over social conduct. In many questions of the responsibility or liability to punishment of any individual either charged with a definitely legal crime, or deemed to be guilty of any important anti-social act, the verdict, be it that of a court of justice or of the sense of social justice alone, must depend more or less on whether or no the accused was fully aware of the nature of the wrong he did, and appreciated the circumstances in which it was done. As a matter of fact, while legal decisions in such cases do often depend to a considerable extent on these considerations, "responsibility" for crime in the wider sense has reference wholly, as Sir James Fitzjames Stephen said, to the law as it ought to be. I have no intention to discuss further the great question of criminal responsibility, but have merely mentioned it now when speaking of the different senses in which the terms "crime" and "criminal" are used and sometimes confused.¹

I purpose, in what follows, to employ these terms generally in the wider sense which I have noted, and to apply the words "convicted criminal," "convicts," or "prisoners" to such offenders who have been *convicted* of law-breaking. It is imperative, in considering the relation of mental defect to crime, to adopt this comprehensive meaning of the word crime. Law of any one period does not cover all actions which are clearly harmful to society; but it must include some actions which the contemporary social conscience would not regard as criminal offences—e.g., some breaches of police regulations, &c. In dealing, however, with the question of mental defect as a factor in criminal action, or in the production of criminal men in the mass, it is possible, convenient, and, for many purposes, sufficient to take under survey only such criminals of all kinds as have been convicted and punished as law-breakers. But we must always bear in mind that large numbers, similarly criminal, are not detected, and that, especially among persons of so-called superior education, there are many whose offences have been spread over several years before detection leads to conviction. Such persons may well be regarded as habitual criminals. But the present law relating to habitual criminals (The Prevention of Crime Act, 1908) provides that no one is amenable to preventive detention unless he is charged with being an habitual criminal simultaneously with a charge of having committed a fresh offence. And for this purpose the term "habitual criminal" is strictly defined in this Act.

At the outset of my last lecture I indicated that a significant proportion of convicted criminals, as compared with the average population, are shown to be either certifiably insane or the subject of such pro-

¹ For a clear and highly instructive consideration of "Criminal Responsibility" involving the question of the law as it is, and the law as it ought to be, there is, I think, nothing better than Sir James Fitzjames Stephen's "History of the Criminal Law," and Dr. Mercier's work on "Criminal Responsibility" (1905), with comments on the former book.

nounced mental defect—evidenced by their general conduct, apart from consideration of the particular crime of which they are convicted—as to need special control. The popular inference regarding criminals who have committed homicide or any specially revolting or apparently motiveless crime, that they are “out of their minds,” is often corroborated by facts observed after their arrest or soon after their conviction. And in many other cases of crime of all kinds and degrees of gravity insanity or other form of mental defect is frequently recognised by medical officers when criminals come into prison after a trial during which no such defence had been raised. It must be noted here that besides the cases of certifiable insanity above mentioned it has been computed by various observers of much experience in the convict prisons that there are from 10 to 20 per cent. of men convicted of crime serious enough to entail sentences of penal servitude of from three years and upwards who are quite incapable of any conduct which would fit them for any form of social life, and are devoid of such mental qualities as would prevent them yielding to common temptations to do some kind of harm to others. Many or most of these cases are doubtless referable to the group of mental defectives generally recognised as congenital in origin. Now, though I am by no means intending here to attribute to this group any special character relative to the origin of their defect, which may not exist in some degree in all other less-marked cases of mental defect, I urge that taking this group and the technically “insane” group together, there is ample justification for regarding the mental disease, disorder, or defect which is inferred as existing in these cases, to be the chief cause of the criminal conduct displayed. In all forms of mental defect the orderly control over the action of the human organism is lessened or deranged or absent; and this fact alone is adequate to explain many criminal actions, all of which involve the predominance of instinctive and other self-regarding motives over those acquired motives which serve to regulate the conduct of the major part of the community which avoids, or is not convicted of, crime. This striking association in many cases of mental defect and disorder with the commission of crime, as well as the inference that defect and crime stand in direct relation as cause and effect, are recognised explicitly or implicitly by most students of criminals, and this matter needs no further exposition. Thus far, we see that an important part played by mental defect in the production of a certain proportion of criminals is clearly illustrated by a mixed group of prisoners whose criminal conduct may be regarded as often and to a large extent referable to pathological or aberrant conditions of organic origin, issuing, with respect to their mental results, in the form of evident loss of duly integrated nervous control. While the make-up of everyone is the outcome of his inborn capacities and of the influences exerted on their development by use and experience—or “education” in its most comprehensive sense—the majority of these defectives may be regarded as mainly the victims of their natural lot.

THE CONDUCT OF THE MAIN BODY OF CRIMINALS.

We have now to consider the case of the main body of criminals: not only those sentenced to long periods of penal servitude: the large majority of whom, probably about 80 per cent., are not the subjects of such a grave degree of mental defect as we have described. The conduct of most of these men does not suggest that they differ greatly or at all in general intelligence from the bulk of the unconvicted population of social grades and circumstances similar to their own. We shall thus now be chiefly concerned with convicted criminals of all kinds and grades who, whatever may be the origin of such mental defect as might possibly, after careful examination, be attributed to them, do not give us cause to regard them as "irresponsible"—i.e., not "rightly liable to punishment" by the law as it is. It is clearly necessary in any endeavour to form an approximate opinion of the rôle of mental defect in the production of crime in general to bear in mind that, although this large class must form the chief material that concerns us, it is practically impossible—mainly because of the very short sentences of most who compose it—to make any such trustworthy study of their individual characters as may be practicable in our convict prisons where the men can be observed for long periods and interviewed frequently. The necessity for bearing this in mind struck me forcibly when reading the interesting work on the "Individual Delinquent," by Dr. William Healy, of Chicago, which contains a mine of information on what may be termed the clinical histories of many criminals. Valuable these histories undoubtedly are, owing to the careful observation and thought employed in their production. But what relation in number these histories bear to any given large number of prisoners who did not undergo such an examination does not appear. The whole collection of cases seems to have been made expressly for the excellent purpose of emphasising the importance of minute study of every delinquent before a just estimate can be formed of the ingredient factors of his crime and of his appropriate treatment, rather than with the object of estimating the extent and force of mental defect per se in producing crime, as compared with that of the extent and force of external influences working on the criminal's inborn capacities.

Since time will not allow me even to sketch an account of the various doctrines that have been promulgated concerning the part played in crime-production by "natural" or inborn qualities on the one hand, and by "nurtural" or environmental influences on the other, I may say here that the extremest views, as formerly expressed by their supporters, are now held by but very few, and that we may practically disregard the exclusive theory of the "born criminal" as held by the one extreme school, as equally discredited with that of the opposite school which taught that the criminal is "made" and is wholly the creature of his social environment, education, and experience.

THE FACTORS OF CRIMINAL ACTION.

In proceeding with the consideration of the factors of criminal action I shall find it necessary to differ only from that opinion which attributes the genesis of crime mainly, if, indeed, not entirely, to certain inferiorities of constitutional or natural origin, and takes little or no account of external influences as bearing on the development of the natural capacities, and consequently, on the actual mental characters of men as we can observe and study them.

My own view, formed after a fair amount of personal experience in the study of criminals, and after giving regard to what can be learned concerning the development of the "mind" from biological and psychological data, is this: the mental make-up of criminals generally, like the mental make-up of all men, depends on the inborn capacities or possibilities of development as well as on the multiform agencies from without which act on this germinal material and may influence its development and give it a bias in many directions. This statement is, indeed, applicable to physical and mental characters generally, and very especially to human mental characters. These must all be regarded as neither wholly "natural" or "constitutional," nor as wholly "nurtural" or "acquired" in origin; they are always the product of both of these factors, though doubtless in varying proportions in different cases.

Regarding as I do the process of development of the human mind as having an essential bearing on the special matter now under consideration, I find reason for making the following condensed quotations in illustration of what I have said. Sir Ray Lankester, in his presidential address on the Advance of Science to the British Association in 1906 said, while speaking of the science of psychology:—

"The most important general advance in this science seems to be the recognition that the mind of the human adult is a social product; that it can only be understood in relation with the special environment in which it develops, and with which it is in perpetual interaction."

Lankester says further, in quoting from a paper he communicated to the Biological Society of Paris in 1899:—

"In discussing the significance of the great increase in the size of the cerebral hemispheres in recent as compared with Eocene mammals, and in man as compared with apes, I came to the conclusion that the power of building up appropriate cerebral mechanisms in response to individual experience or what may be called 'educability' is the quality which characterises the larger cerebrum, and is that which has led to its selection, survival, and further increase in volume. The character which we describe as educability can be transmitted; it is a congenital character. But the results of education cannot be transmitted. In each generation they have to be acquired afresh. On the other hand, the nerve-mechanisms of instinct are transmitted. they are not acquired by the individual in relation to his particular needs."

And Sir Archdall Reid wrote on similar lines in his book "The Present Evolution of Man," published in

1896, and later in the "Laws of Heredity" in 1907. In the latter, when speaking of the development of mind, Reid maintains, by an array of evidence, that the great peculiarity of the human being as compared with other animals is that the distinctive characters of his mind arise much less, as he expresses it, under the stimulus of nutriment alone, and much more under that of use and experience; that his instincts are fewer, while his capacity for making acquirements is infinitely greater and more variable; and that since nature has rendered man transcendently responsive to the "nurture" of use and experience, the question, so often asked, whether "nurture" or "nature" plays the most important part in the development of the human mind has really but little meaning.

To return now to the subject of criminals. With respect to some, of whom I have already spoken, the dominance of the mental defect (which I suppose all observers, whatever their views may be as to the factors of crime, will regard as natural or constitutional, unless there be reason to attribute it to some other process acting on the individual after conception), appears so prominent as to render insignificant any consideration of the action of the environment. But, generally speaking, I believe that in studying the various mental qualities of man as we recognise them it is impossible so to handle them for the purpose of any investigation as simply constitutional or inborn, and taking no account of the external influences on their actual development, which I hold must have a large share in the formation of the mental quality or character in question. Whether this view be correct or not, it must apply to the study of criminals in the mass as well as of any other men; and, on the assumption that it is correct, it is justifiable to say that with some exceptions, already noted, it is not practicable to assess with any precision the proportionate influences of the two necessary factors of "heredity" and "environment" in the development of the minds of criminal men. With the exception, then, of a certain minority of criminals who are the subjects of a high degree of mental incapacity in some form or other, I am of opinion that the bulk of convicted criminals are not so defective in mind as to prevent their criminal conduct, which is without question partly the expression and result of their inborn mental capacities, from being regarded in respect of its origin in the same way as the conduct and mental qualities of all other men would be regarded, psychologically or biologically. This view was based mainly, but not wholly, on my observations of many prisoners convicted of serious crimes and sentenced to long terms of imprisonment, the large majority of whom did not evince any marked signs of grave mental defect either by their conduct or their talk; I thus found further reason to question the solution of crime production by the theory of constitutional defect per se.

From about nine years ago, when the new Preventive Detention Prison at Camp Hill in the Isle of Wight was ready to receive habitual criminals sentenced under the Act of 1908 for "the prevention of crime," in the course of my joint work with some others in advising the

Home Office in the matter of releasing some of these convicts on a special and strict licence I have had much increased opportunity of lengthy interviews with large numbers of prisoners who, from the quality of their records alone, might well be reckoned among the worst of their kind. Among these men it might be expected by many to find a considerably greater percentage of mental defectives than in other collections of prisoners. They had all served previous sentences of penal servitude, some of them as many as four or five, and a considerable majority of them had begun their career of crime in childhood or early youth. The conditions of their detention allowed of more freedom and of far more frequent and intimate observation by the governor and the medical staff and others than are possible in the ordinary prisons. A return recently given to me by the medical officer, Dr. James Murray, of the "mental cases" of various kinds that have been classed as such in this prison shows that out of 475 prisoners of the habitual class I have described who were received from the courts since 1912, 29 were regarded as unquestionably defective, 11 of whom were certified under the Mental Deficiency Act, 1913; 6 were placed apart as doubtful cases and at the time of the return were still under special observation; and 14 were certified under the Lunacy Act as insane. Roughly, the percentage among these men is a little over 10 with various kinds of definite mental defect—i.e., less than the average estimate made of such cases among prisoners generally. These figures, applying only to cases of a prominent kind, have no great value in regard to the question of the mental powers of convicted prisoners as a class in comparison with those of the general law-abiding population; but they are very significant in so far as they show that a *special group* of 475 recidivist convicts, many of them with records of an abundance of serious crimes and of lives of which more than half had been spent in prison, was not more numerously signalled by definitely recognised mental defect than the less selected mass of prisoners in general.

STATISTICAL STUDY OF THE ENGLISH CONVICT.

In my further consideration of the part played by "mental defect" as a factor in the production of criminals, it is necessary to make some comments on the extensive and well-known work by the late Dr. Charles Goring, entitled "The English Convict—A Statistical Study," published by the Government in 1913, and again, in an abridged form, in 1919. This work had its origin in a certain number of anthropological observations made by Dr. G. B. Griffiths, of Parkhurst Convict Prison, some 19 years ago, mainly directed towards checking the facts alleged and the conclusions arrived at by the school of criminologists generally known as followers of the Italian writer, Cesare Lombroso. In process of time these observations were continued by other medical officers of prisons, but at last the scope of them was much extended, and the further conduct of the work was handed over entirely to Dr. Goring, who had followed Dr. Griffiths at Parkhurst Prison. The com-

pleted sets of very numerous observations made on a total of 3000 convicts were then tabulated and dealt with biometrically by Dr. Goring at University College, London. The immense amount of laborious care and ability displayed in this work is widely recognised, and the value of the information it contains is undoubtedly great. Its reputation, moreover, makes it impossible now for anyone who touches on this subject to pass it by without due attention; and I regret that owing to the limit of this lecture, I must perforce confine myself only to some points in this treatise on which I differ from the author. Still more do I regret the incident that a controversy on those points was still proceeding in the *Journal of Mental Science* between Dr. Goring and myself when, last year, almost simultaneously with the publication of my reply to him, I received the unexpected and grievous news of his death.

The object of this extensive research is stated by the author to be twofold: (1) to clear from the ground the remains of the old criminology; (2) to found a new knowledge of the criminal upon facts scientifically acquired and upon inferences scientifically verified. As to the first-named topic no question of the author's methods and results need arise. It is with his handling of the second alone that we are directly concerned. It must be understood that the comments to which I must confine myself cannot approach to a full consideration of the matter dealt with by Dr. Goring under the heading I have mentioned. I can but touch on those parts only which seem to me of paramount importance.

(a) At the outset of this work it is stated by the author that

"it is impossible to assume a priori that the criminal is either 'born' or 'made,' or to what extent criminality results either from a constitutional quality of moral fibre or from purely traditional acquirement." "In other words," he says, "all we can assume, and what we must assume, is the possibility that constitutional as well as environmental factors play a part in the production of criminality. We are forced to a hypothesis of the possible existence of a character in all men which, in the absence of a better term, we call the criminal diathesis." And, further, he says that "we shall have to pursue our research with a mind open to the possibility that innate or constitutional as well as environmental factors play a part in determining the fate of the criminal." Later, in his opening chapter, he expresses the opinion that the conclusion is unavoidable that the "criminal diathesis," although present in greater average intensity among the lawless, is a certain constitutional fact common to the whole of humanity. But the author expressly states that he makes no presumption as to what qualities constitute the "criminal diathesis," the object of his inquiry being "to find out how far, as measured by criminal records, it (the 'criminal diathesis') is associated with environment, and training, with stock, and with the physical attributes of the criminal."

It seems to me after studying these statements repeatedly that this conception of a "criminal diathesis," which is assumed to imply (whatever its component qualities may be shown to be) a constitutional or innate tendency, common to all men but existing in a greater average degree among law-breakers, is

obscure, and tends to confuse the issue of the ultimate conclusion of the argument which is directed towards the founding of a new knowledge of the criminal upon facts scientifically acquired and upon inferences scientifically verified. If this assumed and innate factor of a criminal diathesis were not resolved, as we shall presently see it has been resolved, to a certain extent, by the author into its component elements, it would amount to little more than a statement to the effect that the greater the constitutional tendency to crime, the greater would be the actual commission of crime. With this statement all could agree; it would be self-evident, though not elucidatory. We shall presently find, however, although further factors in the make-up of criminals are set forth by the author in this investigation as differentiating them from the non-criminal population, that one of those differentiating factors is an increased possession of wilful antisocial proclivities. So that the constitutional item of "wilful antisocial activities" comes in to form one element, apart from the others, in the definition of the "criminal diathesis"; and this diathesis itself is posted at the outset as constitutional or innate.

With part of what is said in the quotations I have just made I am in accord. I, too, start with an assumption, not of the "criminal diathesis" described by Dr. Goring as necessary to his argument, but of the position that all men are potential criminals, given the stimulus or temptation adequate to induce antisocial action. I think this is an inevitable assumption. No matter how "advanced" the state of "civilisation" or moralisation, or however great the so-called "social instinct," or, as I prefer to call it, the instinctive tendency to imitate and follow the majority may be, each individual human animal must still make efforts to keep his social conduct up to such a mark as to maintain within due bounds his primary and self-regarding desires and impulses. A man that can acquire and retain this faculty will, as a rule, avoid crime; and he will necessarily be the possessor of a better organised brain and nervous system than the man who cannot. The absence of the inheritable factor in the production of a criminal or of an average moral man is alike inconceivable. I have already enlarged on this point in my first lecture, where I also insisted on the coöperation of other factors as equally necessary, also in varying degree, to the production of the observable characters of nearly all men—i.e., of all men described precisely by the author of the "English Convict" as "normal," including, of course, criminal men. And just as under sufficient stress the tendency of the human brain to become disordered may be demonstrably actualised, so may a breakdown take place in that subtle mechanism which underlies and actuates the conduct and characters of men.

(b) The contents of Dr. Goring's work consist of a minute and wellnigh exhaustive study, by means of the biometrical method of statistics, of the following matters, relevant to his inquiry, and bearing closely on his exposition of what he terms the "criminal diathesis." These consist of (1) the physique of

criminals; (2) age as a biological factor in crime; (3) the criminal's vital statistics—health, disease, mortality; (4) mental differentiation of the criminal; (5) the influence of the force of circumstances on the genesis of crime; (6) the fertility of criminals; and (7) the influence of heredity on the genesis of crime.

FACTORS OF CRIME PRODUCTION.

As a final result of the examination of his extensive observations under each of these headings the author arrives at the following conclusions:—

(1) "That there is a physical, mental, and moral type of normal person who tends to be convicted of crime—i.e., that, on the average, the criminal of English prisons is markedly differentiated by defective physique, as measured by stature and body-weight; by mental capacity, as measured by general intelligence; and by increased possession of wilful antisocial proclivities, as measured, apart from intelligence, by length of sentence to imprisonment." (2) "That relatively to the origin in the constitution of the malefactor, and especially in his mentally defective constitution, crime is only to a trifling extent (if to any) the product of social inequalities, of adverse environment, or of any other manifestations of what may be comprehensively termed the force of circumstances."

It is clear that these conclusions must be accepted, provided that the premisses are not questionable. But the premisses, in so far as they concern the mental element in the production of crime, involve the postulated assumption: (1) that the factor of "mental defect" stands for defect of intelligence alone and is of innate origin; (2) that the remaining factor, described as "increased antisocial proclivity," is also of innate origin; and (3) that these two innate factors have been correctly established as at least predominant or as sole factors in crime production by the exclusion of all significant external influences which, as the author himself has said, ought to be regarded at the beginning of an inquiry as *possible* factors in determining the fate of the criminal or, in other words, as part factors of the criminal diathesis.

That I am of opinion that Dr. Goring has not succeeded in estimating "mental capacity" by his method of measuring "general intelligence" or, consequently, of establishing the wholly constitutional nature of "mental defect" will be apparent from what I have already said. As regards the factor of increased possession of wilful antisocial proclivities as measured by length of imprisonment, it seems to me that under this title are gathered other characters, generally regarded as mental by psychologists, but not reckoned as such by the author, and expressly excluded by him from his own concept of "mental defect." He regards this innate or "constitutional" factor as in a great degree concerned with the criminality of such malefactors as are not significantly characterised by either defective physique or defective intelligence, but only by the possession in excessive measure of this assumed innate quality which is not otherwise defined, and appears to me to lack any explanatory value. Surely apart from all discussion about "mental defect" as a factor of crime,

wilful antisocial activity is crime. Shorn of his wilfulness the law-breaker is not criminal, though he may be such in the technical sense. But without this assumption of innate "wilful antisocial proclivity" on the part of the considerable proportion of criminals who show no defect either of physique or of intelligence, this class of criminals could not be regarded as the subjects of any constitutional mark relevant to their criminal conduct.

It is because I deem that some of the collected facts as dealt with in this research by the biometrical method are open to much dispute, and consequently entail some very disputable and, in my opinion, erroneous conclusions, that I have thought it necessary to make these comments, believing that the method employed is not fitted to the whole of the material handled by it in this investigation. Much of the material differs widely from that which can be definitely estimated by measurement. In this instance, indeed, the method, as Huxley said concerning another method and another matter, "may be compared with a mill of exquisite workmanship which grinds material to any degree of fineness, but what comes out of it depends upon what is put in."

While believing that in the production of the great majority of convicted criminals of all kinds an important part is played by the innumerable and often unobservable influences from without on the development of each individual's mental capacities, and thus on his conduct, I do not question the conclusion arrived at by a different route in "The English Convict," that convicted criminals are, as a body, of inferior intelligence to that of the average members of the community. Indeed, this is probably true of the mass of convicted criminals everywhere, who as a body, in the local prisons all over the country, give the impression to those conversant with them that they are more stupid than the majority of people of a similar status. Considering that a very large number of crimes are committed without detection of the perpetrators, it is at least highly probable that convicted criminals would be on the average much less alert, mentally, than those who succeed in eluding the police.

CONCLUSION.

I trust that in these lectures I have made it clear that my object has been to give reasons for my opinion that criminal conduct is dependent on the innate capacities of each individual as developed and actuated by the innumerable influences which act upon these capacities; and that the actual mental characters or qualities that we observe are the resultant of these factors. My position has been seriously misrepresented as an appeal to the emotions in favour of the notion that crime is wholly the product of environment, and as a denial of the part played by the constitutional or innate factor in the make-up of the criminal. But in stating my judgment that a theory of criminality which virtually excludes environmental influences in the development of the mental, moral, and social qualities in man, would necessarily lead to such a conception of crime as would

logically, and I think practically, tend to discourage active measures directed towards reclaiming the criminal, I am not influenced, as has been suggested, by any consideration whatever as to the *consequences* of this or any other theory, but solely by my belief that this theory itself lacks both scientific truth and probability.

In my opinion the proper and fruitful understanding and treatment of criminals depends mainly on the careful study of the individual offender. I am further of opinion that this consideration should influence far more than it does at present the sentences awarded in courts of law, which are to an undue extent based on the class of crime committed, irrespectively of the history of the accused person, and of the circumstances in which the offence took place. I think, further, that no judge should pronounce any sentence of imprisonment unless he is personally acquainted by visiting prisons with the actual nature of the terms of imprisonment entailed by his sentences.

An Address
ON
THE NEUROLOGICAL ASPECTS OF
SHOCK.

*Delivered before the Leicester Medical Society on
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SHOCK may be defined as a condition of profound exhaustion and prostration of voluntary and involuntary functions of acute onset, caused by trauma, surgical operations, or sudden emotional or commotional disturbance of the central nervous system, or to the effects of toxic agents and anaphylaxis. The term has unfortunately been greatly extended by the inclusion of all forms of war neurosis under the name of "shell shock," the symptoms of which in no way differ from cases that have never been exposed to shell fire. It will be my endeavour to show that over-stimulation and exhaustion of the central nervous system play an important part in the production of all forms of shock.

PRIMARY AND SECONDARY SHOCK.

Two forms of shock may be recognised : (a) primary ;
(b) secondary.

Primary shock.—This form is analogous to a faint or collapse coming on instantaneously as a result of emotional or commotional disturbance of the brain. It may come on immediately on receipt of an injury, but in some instances when the patient actually sees the injury, showing that the emotional disturbance was the cause and not the injury.

Secondary shock.—The late onset of secondary wound shock does not refute the theory that surgical shock may be the result of over stimulation by nociceptor afferent impulses exhausting the vital medullary centres presiding over the circulation and respiration ; but it allows of the conception that other factors—namely, the *toxic*—play an important part in its causation, for in secondary shock the necessary time for the production and absorption of toxins would occur.

Before passing on to discuss the two forms of primary and secondary surgical shock it is necessary to make a few remarks upon anaphylactic shock.

Anaphylactic Shock.

Prior to the discovery of anaphylactic shock by Richet it was the fashion to ascribe all the "shock" effects of the ingestion of harmful substances into the body to toxæmia. Anaphylactic shock is characterised by dyspnœa, fall of blood pressure, vomiting, and other gastric intestinal disturbances, accompanied by collapse, and in some cases by convulsions, a symptom-complex which follows the administration of any one of a large number of dissimilar substances of animal or mineral origin to which the blood and tissues is inherently over-sensitive, or has been rendered over-sensitive by previous administration.

These symptoms, according to Widal and his collaborators, are accompanied and preceded by a "blood crisis" of remarkable suddenness and intensity characterised by a leucopenia with predominance of lymphocytes, diminution of blood platelets, and great alteration in coagulability. They propose to call this condition hæmoclasia, the term implying a sudden dislocation of the static equilibrium of the colloids of the blood—a bio-physical manifestation—and this was the conclusion arrived at by Bezredka in 1907. But the physics and chemistry of the colloids, about which at present we know but little, underlie all vital phenomena, and it may be presumed that in anaphylactic shock there is a dislocation of the static equilibrium of all the cells of the body, especially of the nervous system, and the term colloidoclasia would more accurately represent the condition. Idiosyncrasy may be regarded as a specialised inherent hypersensitiveness to the dislocation of the static colloidal equilibrium from the action in the body of particular substances.

THE FALL OF BLOOD PRESSURE IN ALL FORMS OF SHOCK.

In all forms of shock there is a fall of the blood pressure, and when death takes place it is by a failure of the vital autonomic centres presiding over the circulation and respiration. Now, in shock, which comes on some time after injury, this question arises: Do these vital centres fail to function, primarily on account of exhaustion through over-stimulation, or do they fail secondarily from (1) the effects of toxins, (2) from fall of blood pressure and consequent anæmia, or (3) from exæmia with concentration of blood and capillary stasis in some cases accompanied by fat embolism?

In my opinion there is evidence to show that in secondary shock from extensive burns and severe wounds, especially compound comminuted fractures with extensive laceration and injury of the soft parts, all the before-mentioned factors conspire together to form a vicious circle, which tends to a fatal termination by failure of the vital autonomic centres presiding over circulation and respiration. In fatal primary emotional or commotional shock toxin absorption cannot play a part, for the symptoms immediately follow the exciting cause; and a fatal termination can therefore only be due to a refractory or exhausted condition of the vital autonomic centres presiding over the circulation and respiration.

PRIMARY SHOCK AND THE PSYCHONEUROSES.

What is the psycho-physiological explanation of emotional shock? We know that a sudden emotion may cause a "faint," a sudden loss of consciousness explicable by a sudden fall of blood pressure. Now, if the fear stimulus which caused this persists there may be a continuance of arrest of function of the autonomic centres; and in very rare cases a fatal termination has been known to result. Individuals who are inherently neurotic or of a timorous temperament, or persons whose higher controlling centres have been exhausted by prolonged stress, anxiety, and insomnia, are most susceptible to emotional shock.

In the great majority of cases of primary commotional and emotional shock after a variable time the patient recovers. In hysterical patients some part of the field of consciousness may remain dissociated, and the result is mutism, psychic blindness or deafness, paralysis, tics, tremors, contractures, &c., all of which can be readily cured by suggestion or persuasion. Not infrequently following the emotional shock the patient remains for a time in a dazed or semi-automatic state. He has no recollection of what transpired during this period of his life. It may happen that he does not recollect the events which immediately preceded the shock; and I have seen cases in which the shock was so severe that the memory of all past events of their life were blotted out, and in several cases of this kind they spoke only a few simple words in an infantile way, both as regards the words used, the mode of articulation, and the modulation of the voice.

Now, two types of psychoneurosis may follow emotional or commotional shock—viz., hysteria and neurasthenia; the former was the commoner in the ranks, the latter much the commonest in officers. Hysterical symptoms arising from auto- or hetero-suggestion were curable by contra-suggestion. They were the result of a preservation of an unconscious wish-fulfilment to avoid an intolerable situation; a defence mechanism related to the emotion of fear. The other form of psychoneurosis, which may follow emotional or commotional shock, is neurasthenia—irritable nervous weakness with mental preoccupation, concerning a situation for which the man is unable to make fitting necessary mental adjustment. In the case of officers there was a continuous mental conflict between the impulse to return to duty, fearing otherwise that they would be considered either cowards or scumshankers, and the fear of returning to an intolerable situation, not always intolerable on account of the danger to life, but intolerable because they felt they did not possess the will-power and energy to undertake efficiently duties and responsibilities involving the lives of their men. This mental conflict, combined with insomnia and unrefreshing sleep accompanied by terrifying dreams, together with the effects of previous stress and strain of war can exhaust the vital energy of a good soldier and render him more susceptible to either primary or secondary shock.

Now, one of the problems medical officers in the Great War had to decide was whether a case of shock

should be classified as a battle casualty. Was the patient sufficiently near a large shell when it exploded to cause commotional shock? Especially would such a classification be justifiable if the man were buried, or if the shell burst in a dug-out, or closed space, where the effects of repercussion would be felt and if he had signs of contusion on the body. Still, many individuals with an inborn or acquired emotivity might suffer so severely from emotional shock that it would be extremely difficult to decide from symptoms whether the case was commotional or emotional. For a man neuro-potentially sound, after prolonged stress, anxiety, and exhaustion of trench warfare, may become emotive. The previous conduct of the man as a soldier, the time he has been on active service at the front prior to the occurrence of the shock are important indications. If when he recovered consciousness there existed a retrograde amnesia and he exhibited neurasthenia and not hysterical symptoms it may be presumed that the case was one of commotional shock. Observations, moreover, show that in commotional shock, as distinct from purely emotional shock, the cerebro-spinal fluid exhibited an increased pressure when lumbar puncture was performed; it has also been found that the fluid upon examination contained protein and in some cases blood. True commotional shock is, relatively to emotional shock, rare, perhaps 5 to 10 per cent. of the cases of so-called "shell shock."

"COMMOTIONAL SHOCK."

The forces generated when high explosives are detonated are enormous, and men have been found dead from shock without visible injuries to account for it in dug-outs and closed spaces where percussion and repercussion can occur. Undoubtedly there is a condition of true commotional shock, although there is a tendency now almost to decry its existence. The brains of soldiers who have died of commotional shock have been sent to me to examine, and my observations show that this form of shock is a definite condition not met with in other forms of shock which I shall describe. Moreover, Colonel P. W. G. Sargent, in a very interesting introduction to an article on Shock, published by the Medical Research Council, gives instances of two cases of death from shock caused by explosives, in which the brains showed no naked-eye evidence of injury and no fracture of skull. Perhaps if the brains had been examined microscopically similar changes to those which I shall describe might have been found.

Before, however, considering the nature of the different forms of shock, let me call your attention to some anatomical and physiological facts bearing upon the subject of primary and secondary shock.

Anatomical and Physiological Facts Bearing upon Shock.

Referring to the theory of dislocation of the static equilibrium of colloids as a cause of anaphylactic shock, we may ask, may this be an explanation of commotional shock, in which no sufficient visible macroscopic or micro-

scopic changes can be found to account for the symptoms. The study of the living neuron shows that Nissl bodies and fibrils in the ganglion cells are artefacts, the result of death changes, and due to the action of fixatives and stains; for if we look at the living nerve cell by direct illumination, we see an emulsion of black dots in the plasm, in the centre of which is the nucleus; the converse is observed in the cell when examined microscopically; for it seems to consist of a plasm in which are numbers of highly refractile granules of similar shape and size, with a dark-looking non-refractile nucleus, which contains none of these granules. When the living cells are stained with vital blue the granules take the blue stain. If the cells so stained are kept in cerebro-spinal fluid in an atmosphere of N the blue colour fades to a green. This affords evidence that the granules form an oxygen surface like spongy platinum. By the catalytic action of the P and Fa of the nucleus the molecular oxygen on the surface of the granules is continually being converted into atomic oxygen, and this process is fundamental to the life and functional activity of the neuron. Now it is conceivable that a violent commotion, even without contusion sufficient to cause minute hæmorrhages into the nervous substance, may have a profound effect upon these delicate colloidal structures and cause a dislocation of static equilibrium. The force of the explosion may be so great as to be conveyed through the enclosing structures of the brain, and in spite of the special protective water-cushion mechanism of the cerebro-spinal fluid, cause a "shock" to the vital centres of the medulla, and sooner or later a fatal termination; the rupture of small vessels may not be sufficient of themselves to account for death, but are merely an expression of the force of the explosion.

Nissl Granules and Neural Energy in Relation to Shock.

Do we possess methods by which we can ascertain the existence of exhaustion of the neural energy of the ganglion cells and biochemical changes upon which can be established a neuropathological theory of "shock." Now, although the Nissl bodies are artefacts, yet the amount of this basic chromophil substance may be regarded as an index of the amount of stored energy substance; and to continue the argument we must assume that stimuli arriving at the cell excite the catalytic action of the nucleus and the stored latent energy substance is thereby transformed into active energy in the form of stimuli, which are transmitted directly or indirectly to muscles and glands through systems of neurons. Now it is quite obvious that excessive stimulation, when associated with multifarious depressing conditions, may lead to exhaustion by over-stimulation of this latent store of neuro-potential; and particularly is this likely to occur if there is a fall of blood pressure accompanied by other contributory factors, especially pain and loss of sleep, during which neural energy is stored. Crile's experiments show that an exhaustion of the kinetoplasm may occur from absence of sleep.

Crile's Theory of the Inter-relation of the Brain, the Thyroid, and the Adrenal Glands in Relation to Shock.

Crile maintains that there is an inter-relation of the brain, the thyroid, and the adrenal glands. He puts forward the theory that "through the special senses and common sensibility environmental stimuli reach the brain and cause it to liberate energy, which directly or indirectly activates muscles and glands, among others the thyroid and adrenals." The thyro-iodin is essential for the storage of neural energy.

The clinical symptoms of myxœdema show this, and I have found in seven cases of myxœdema a great diminution of this basophil-staining substance of the neurons, especially affecting the autonomic cells of the medulla.

The work of Cannon and Elliot has shown that in anger and fear there is an increased quantity of adrenalin discharged into the circulation. The instinctive protective reaction in a struggle for life in man is either fight or flight, both of which require an increased production of energy in the whole neuro-muscular mechanism. The store of adrenalin in the suprarenal gland is a defensive mechanism for emergencies connected with the instinct of self-preservation. Not only does the substance raise the blood pressure; it stimulates oxidation processes, mobilises the glycogen in the liver as sugar, and increases the coagulability of the blood; and it also excites the discharge of thyro-iodin into the circulation. This automatic pouring out of adrenalin and thyro-iodin is brought about by an excitation of the autonomic centres in the medulla conveyed to the suprarenal glands by the splanchnic nerves. In persistent paralytic fear or persistent psychic shock there is a continued emotional refractory reflex condition of these medullary autonomic centres causing establishment of a vicious circle connected with the normal storage and discharge of neural energy. This condition is much the more likely to occur in trench warfare than in a war of action; for the soldier exhausted by prolonged stress of enforced inactivity, unable to fight or run away, the two instinctive protective reactions to threatened dangers, has to adopt the paralytic crouching attitude of concealment.

Having thus dealt briefly with the psychic mechanism of emotional shock I will pass on to a description of the morbid changes found in "commotional shock"; but it must be obvious that a man whose neural energy has been exhausted by stress and strain and has become neurasthenic is more likely to suffer severely and die from shock caused by the explosion of a large shell near him than a man whose neural energy is not in a state of exhaustion. The following case illustrates this point:—

Case of Commotional Shock and the Microscopic Findings in the Brain.

A soldier developed nervousness, owing to the severe stress of fighting on the Somme, which he never lost, but was able to control for six months. Later he was in an area which was subjected to an intense bombardment, during which, as far as can be ascertained, no gas-shells were used; this lasted about four hours. Although he remarked to another man "he could not stand it much longer," he did not give way until the following day, 12 hours later, when perhaps six shells came over. He was not buried and not gassed. One burst just behind his dug-out—viz., 10 feet away—in the morning, but many must have been as near the previous day. Early symptoms were general depression and tremors. The later symptoms were coarse tremors of the limbs, crying, inability to walk or do anything. He could not answer questions and his pupils were dilated. The condition of the pulse is not noted. The M.O. who made this report states that he was very busy with wounded at the time, and unfortunately did not make a detailed examination. He was admitted to F.A. in the evening in a state of acute mania, shouting "Keep them back." He was given two hypodermics of morphia and chloroform and slept all night. Next morning he woke up apparently well

and suddenly died. It cannot be said that the clinical notes are very satisfactory, and from the correspondence it appears that there was some difficulty in obtaining them. The report of the P.M. examination by Captain Adrian Stokes is completely satisfactory. I will do no more than give his conclusion. "There was no gross lesion of the viscera, which would have been a cause of death, but though I have never seen a case of 'shell shock' I consider the condition of the brain is consistent with that diagnosis." The notes state there were no external marks of violence on the body other than some small scratches on the chest wall. The lungs were oedematous, and in the substance of the lower lobe of the left lung there was a hæmorrhage.

Head.—There was a slight bruise on the scalp in the frontal region. The brain was extremely congested, and on each side of every vessel there was an ecchymosis. There were a number of minute punctiform hæmorrhages at the termination of the smallest vessels on the surface of the brain. The whole brain was soft, but not markedly oedematous. The cerebro-spinal fluid appeared to be tinged with blood. There was no large hæmorrhage found and no small intracerebral petechiæ.

It may be remarked that hæmorrhage into the lung has been found in animals exposed to the force of detonated high explosives and a similar condition of the brain.

The main interest of this case is that there was no complication of gas poisoning; in the other two cases this cannot be excluded, and probably existed for the punctiform hæmorrhages found in the corpus callosum, and white matter is found in CO and other forms of gas poisoning due to thrombosed vessels. In the white matter of the corpus callosum, the internal capsule, the basal ganglia, the pons and medulla there are seen congested veins and hæmorrhage into the sheaths of the vessels; and in the lower part of the medulla oblongata a vessel has ruptured, not only into the sheath of the vessel but into the adjacent nervous tissue. Inasmuch as in this case death in all probability resulted from heart failure, it may be associated with the changes observed in the cells of the vagus nucleus. The macroscopic and microscopic appearances of the brain are consistent with fall of blood pressure and cerebral anæmia.

CEREBRAL ANÆMIA AND SHOCK.

I have found that certain similar conditions indicative of cerebral anæmia exist in the brains of all cases of fatal shock, whether primary, due to shell concussion, or secondary shock following cases of (1) extensive burn, (2) severe gunshot wounds with fracture of bones and much laceration of tissues, and (3) contusion of heart and slight gunshot wounds. In most instances there was a wet condition of the brain; in a few cases the superficial veins were noted as being congested at the post mortem. I have observed similar conditions in the brains of animals after ligation of all four vessels. They indicate a deficiency of blood in the brain, its place being taken by cerebro-spinal fluid.

MICROSCOPIC EXAMINATION OF BRAIN IN SURGICAL SHOCK.

Microscopic examination revealed in all these cases of shock (1) many empty collapsed vessels in the substance of the brain, with dilatation of the periadventitial spaces and perineuronal spaces, both of which are filled with cerebro-spinal fluid; (2) a variable degree of chromatolysis of the brain cells, most marked and obvious in the autonomic nuclei of the medulla oblongata and less marked in the bulbo-spinal motor nuclei—e.g., the hypoglossal and cervical spinal motor cells; (3) the smaller pyramidal cells of the cortex are, as a rule, more affected than the large pyramidal and Betz cells; (4) the cells of Purkinje have shown definite chromatolysis and a tendency to take the eosin-acid staining dye in place of the blue basic dye. This confirms the observations of Crile, who noted this change of staining reaction in all forms of shock, whether in human beings or as a result of experimental conditions in animals.

Why does this occur with such constancy and intensity in this organ of uniform structure? There are many biological and physiological facts in support of the view that one, and perhaps the most important, function of the cerebellum is that of a large store of neural energy for reinforcing muscular action. The acidophil reaction which Crile found that these cells manifested, he used as one argument in favour of "acidosis" in the production of shock. In the very remarkable and extensive series of researches which have been carried out under his direction, attention has been directed only to the cerebellum. Other cells of the central nervous system do not show this acidophil reaction. But that "acidosis" is an essential factor cannot be claimed for intravenous injection of alkaline. Locke or Ringer's fluid does not prevent a fatal termination in cases of shock.

Fat Embolism in Surgical Shock.

Porter examined the brains of a number of cases of surgical shock caused by extensive gunshot wounds and found fat embolism. He came to the conclusion that this might be the cause. I have found fat embolism in three cases of gunshot wound with compound comminuted fractures of large bones and much damage and laceration of the soft tissues, but I do not think it was sufficient to cause a fatal termination, although it may have been a contributory factor, seeing that vessels in the medulla contained droplets of fat.

Absorption of Histamines in Surgical Shock.

A more important cause of secondary wound shock is the absorption of histamine or toxic substances from the damaged muscles. The arguments advanced in favour of the absorption of toxins derived from damaged muscles are: (1) A number of these men suffering from pure muscle injury have died of shock. It has been established that microbic infection is not an

important factor in these cases. (2) Great improvement may follow rapid amputation of a lacerated limb. (3) Bayliss has shown experimentally that violent damage of the muscles of an animal while under anaesthesia causes shock; but Crile would argue that when you damage a tissue, although that animal may not show any signs of feeling, it is nevertheless receiving nociceptor stimuli, and it is quite conceivable that these nociceptor stimuli reaching the great central station for pain, the optic thalamus, are unconsciously reflected down to the cardiac and respiratory medullary centres. Morphia, carefully administered—and it may be remarked that it is contra-indicated if there is cyanosis—will relieve pain and excitation of the nerve centres and help to prevent shock in severe wounds.

Experiments of Dale on Histamine Shock.

There is experimental evidence that absorption of toxins derived from damaged tissues play an important part in the production of shock; for Dale has shown that injection of histamines produces shock. In one case, after slow infusion occupying an hour, death took place from failure of the vital centres. During that time the cells had used up a certain amount of the basophil staining substance shown by the comparison of the appearance of the cells of the medulla and the large flask-shaped cells of the cerebellum with similar cells in the brain of an animal which died three minutes after infusion at once of the same amount of histamine. In this case of sudden death there was no time for the cells to use their stored energy substance; consequently they present a normal staining appearance.

The former experiment would represent what actually takes place in wound shock—viz., a slow poisoning of the vital centres. It may be presumed that in the former there was a slow and progressive fall of the blood pressure; in the latter there was a gradual fall. Four other brains are being investigated.

Vascular Theory of Shock: Exæmia of Cannon.

I have not said anything yet about the vascular theory; it was formerly held that in "shock" the blood pressure fell, owing to its accumulation in the capillaries and veins of the abdominal organs. But it has been found that this is not the case. There is, however, a concentration of the blood and stasis in the capillaries of the body generally, a condition which Cannon calls "exæmia." The plasma exudes through the capillary walls into the tissues; and in proof of this concentration is the fact that the hæmoglobin index is increased, likewise the blood cells count.

TREATMENT OF SHOCK.

Intravenous injection of salines proved useless; in some cases transfusion of citrated blood and gum saline solution, which was introduced on the assumption that

it could not escape from the vessels, have raised the blood pressure and led to recovery ; in others, as in the four cases of which I have investigated the brains, these measures were unavailing. Crile recommends introduction of fluids by natural methods—e.g., Murphy's drip enema of 5 per cent. glucose and 5 per cent. soda bicarbonate solution. Stimulants seem to be useless, also injection of adrenalin and strychnine.

I have already pointed out that all causes of exhaustion of vital energy, whether psychical or physical, predispose to primary and secondary shock. In the case of the wounded in battle, thirst, exposure to cold and wet, delayed evacuation, rough and prolonged transport to hospital, and suffering with acute physical and mental agony conspire together to sap the vital energy, and when in consequence of circulatory failure and toxæmia the vital centres of the medulla become refractory and fail to discharge impulses the blood pressure falls progressively, and eventually in spite of all remedial measures the circulation and respiration cease.

In secondary wound and burn shock I did not find hæmorrhages; I conclude, therefore, that in cases of true "shell shock" this condition is due to physical effects produced by the forces generated by the explosion, but in some cases to the poisonous effects of gases absorbed while the man is lying unconscious.

In resuscitation from surgical shock practical experience shows that the treatment of the following phenomena have yielded satisfactory results—viz., (a) the fall of blood pressure; (b) the fall of the body temperature; (c) the lessening of the volume of the blood. Experience shows that cases of hæmorrhage combined with little shock yield the best results.

In conclusion, I desire to say that a full report of the neurological changes will be published shortly by myself and Dr. Uno, of Tokio, who is at present engaged in making an investigation of the microscopic changes in my laboratory under my direction.

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THE INFLUENCE OF SONG ON MIND AND BODY.

AN ADDRESS⁽¹⁾ GIVEN TO THE VOCAL THERAPY SOCIETY
AT LADY ST. HELIER'S.

By SIR FREDERICK MOTT, K.B.E., M.D., LL.D., F.R.S.

It is now two years since Armistice Day, and I then delivered a short address on vocal therapy and the manner in which it originated at the Maudsley Hospital in small beginnings. It was then energetically supported by Lady Carnarvon, and a society was founded for the purpose of providing teachers for instruction of soldiers and ex-service men in breathing and singing, as well as in the treatment of speech disabilities, under medical direction and supervision. I was fortunate in securing such excellent teachers as Miss Oswald, Miss Bush and Miss Dredge, who, with genuine enthusiasm, successively carried out vocal therapy at the Maudsley Hospital.

Lady Carnarvon asked me if I would (at this third Annual Meeting) deal with the subject of vocal therapy from a popular psychological point of view. I agreed, but I felt that although my remarks would treat mainly of the mental aspect of vocal therapy, I should expand the title to "The Influence of Song on Mind and Body," for in my opinion the two are indissoluble. There can be no mind without memory and no memory without body ; moreover, the furniture of the mind consists

(1) Inasmuch as orchestral and vocal music form an important adjunct to treatment in mental hospitals, I ventured to ask the Editors if they would care to publish it in the *Journal of Mental Science*, for although of a popular scientific character it might prove of interest to many of its readers.

[We gladly publish this address, not only for its literary charm and scientific merit, but because it will assist the public and public authorities more thoroughly to appreciate that music in mental hospitals is not merely "to pass the time" or a form of "kindness to patients," but a valuable adjunct to psychic treatment meriting every encouragement and adequate expenditure.—Eds.]

of past experiences and the bonds that unite them. The Great War has shown the extraordinary influence of the mind on the body when it has been affected by experiences causing contemplative fear, resulting in conversion hysteria in the form of various paralyses, mutism, blindness, deafness, etc., but in this address I intend to explain the psychic mechanism of the voice in relation to the emotions.

MUSICAL MEMORY.

Quite early in the war two cases of true shell-shock amnesia, with complete anterograde and retrograde loss of memory, came under my notice which showed that musical memory usually returns earlier than other forms of memory, or rather the power of recollecting past experiences. I found that these two soldiers suffering with shock, one of whom had been a singer and the other a piano-player, were able to remember and to sing songs or play pieces they had learnt on the piano prior to the shock, and yet were unable to remember experiences connected with their daily avocations and home surroundings.

Again, there were cases of men who were mute from the same cause who suddenly regained their speech at a concert by joining in the chorus of some well-known song.

Moreover, a fact well known before the war, and emphasised by numbers of soldiers and ex-service men afflicted with stammering and stuttering, is that people who suffer with these speech disabilities are able to sing a song without their diction showing this defect.

Now, of all the arts music appeals most to the emotions; and probably the reason why countless men and women who are illiterate and uneducated can recall the words of songs and hymns when they hear the first bar of the musical setting, is that words associated with music are more stably organised in the mind, owing to the musical origin of language. There are, broadly speaking, two psychological laws of association in memory, *viz.*, association by contiguity and association by similarity.

ASSOCIATION BY CONTIGUITY.

In singing a song there is contiguous association of musical cadence and articulate speech. We shall see that there is reason to suppose that the utterance of vocal inarticulate sounds of varying pitch is, evolutionally speaking, much older than articulate speech, and that whereas the production of such sounds can be initiated in both halves of the brain, articulate language in right-handed persons can only be initiated in the left half of the brain, which controls voluntary movements of the right half of the body—a fact that proves that expression of our thoughts by graphic symbols made with the right hand has grown

up and progressed simultaneously with language spoken by means of auditory symbols. Song has been defined by Grove as a short metrical composition whose meaning is conveyed by the combined force of words and melody. The two are organised in the mind simultaneously and each reinforces the other in memory.

The following is a very instructive case considered in relation to the psychological association by which words are revived (in a case of aphasia) by melody. A soldier came under my care who suffered with aphasia and paralysis of the right side of the body in consequence of a gunshot wound of the brain.

The bullet entered the left side of the head and passed through the left fronto-central region of the brain, damaging the motor speech centre, probably together with its connections with the auditory word centre, and through the right orbit, destroying the eye; in its passage also it must have cut through the left optic nerve or tract, for he was totally blind. This poor fellow was very cheerful and comprehended all that was said to him; thus, by feeling my tunic sleeve he recognised my rank, for when asked if I was a captain he expressed negation by "Oot," meaning "No," and major by "Ah," which was correct at that time. He obeyed all commands. Now, curiously enough, although he was able to express judgments only by "Ah" and "Oot," which corresponded to "Yes" and "No," he was able to sing several songs through without difficulty, provided the first word or bar of music was given. Thus, I stood beside him and hummed, "'Tis a long, long way," and immediately he started the well-known chorus of "Tipperary," winding up with "Are we downhearted? No!" I then said, "Say Tipperary, Tom." He replied, "Oot," and he was unable to utter any of the words. It must be concluded either that the song had been repeated so often as to have become organised in both halves of his brain or in subcortical lower centres. We know also that in amnesia (loss of memory) rhymes are recalled very easily, especially if they have been learnt in early life. A month later, when I saw him, he was able to walk and speak. Thus, given half-a-crown, he felt it, then tried the rim for milling with his teeth, and said, "Two-shilling-bit." Then asked again he corrected it with "Half-crown." Given a penny he tested it in the same way, and the unpleasant taste left in his mouth caused him to throw it down with all the signs of disgust, saying, at the same time, "Copper."

ASSOCIATION BY SIMILARITY OF SOUND.

Association by similarity is illustrated in rhymes which are easily remembered by similarity of sound. Popular metaphor speaks of "Rhyme without reason," for the association is superficial and does not imply deliberation and judgment; it is the first to come in mental evolution and the last to go in mental decay. An interesting example of this was afforded in the case of a woman suffering with alcoholic dementia who had complete loss of memory for recent events and mental confusion. I told her that the name of the superintendent of the asylum was Dr. Jones. She immediately added: "Broke his bones, falling over cherry stones." A few minutes later I asked her the name of the superintendent and she had quite forgotten. But when I mentioned "Cherry stones" she replied: "Oh, Dr. Jones," and the rest of the rhyme was repeated.

THEORIES OF THE ORIGIN OF MUSIC AND LANGUAGE.

Herbert Spencer, in an essay on the origin and function of music, on the one hand came to the conclusion, like Diderot, that the cadences used in emotional speech afford the foundation from which music has been developed; on the other hand, Darwin concluded that musical notes and rhythm were first acquired by the male and female progenitors of mankind for the sake of charming the opposite sex. Thus, as he says, musical notes became firmly associated with some of the strongest passions and are consequently used instinctively, or through association, when strong emotions are to be expressed in speech. This explanation is certainly true, but it does not cover completely the origin of speech, for the language of the emotions, which is a universal mode of expression of feeling, is based upon the expression of the desires and the satisfaction and attainment of ends ministering to the three primal instincts—the preservation of the individual, preservation of the species, and the herd instinct. This language of the emotions and passions is accomplished by gestures and facial expressions accompanied by modulated inarticulate cries of varied pitch and loudness. Darwin gives many instances of birds and animals that flock together giving warning signals to their flock or herd of approaching danger. Again, the cry of the young animal for its mother and the answer show that variations of pitch in the cry are employed as a means of preservation of the individual, a cry for help or food. Experience shows also that there is an individuality of the cry of the offspring and reply of the mother in a flock or herd—a cry of recognition.

It is more probable that an inarticulate language of emotion preceded articulate language, and being much older evolutionally, is consequently dependent upon a more stable preorganised mechanism, represented in both halves of the brain. Indeed, whereas stimulation of the laryngeal centre excites movement of both vocal cords, stimulation of the tongue centre excites only the muscles of the opposite half of the tongue. The conscious movement of the jaw, the tongue and the lips, the articulatory mechanism of speech, are under the direct control of the will. The movements of the muscles controlling the tension of the vocal cords are unconscious and are not under the control of the will, but are directed solely by the sense of hearing, which is the primary incitation to phonation. But phonation is essential for articulate speech, therefore hearing is the primary incitation to articulate speech. A child that has acquired speech at two or three years of age, who subsequently becomes stone deaf from middle-ear disease, later in life loses the power of articulate speech. Mutes, when once they are made to phonate, recover their speech, generally almost immediately. My experience, in a large number of cases of hysterical mutism in soldiers, was that as soon as

ever they could be made by suggestion or Faradism of the larynx to cough with tone, showing the vocal cords were approximated, speech returned and they were cured. The functional dissociation of the bilateral cortical phonating mechanism had been overcome by this instinctive act of coughing.

SIMILARITY OF EMOTIONAL LANGUAGE IN DIFFERENT RACES.

There is a close similarity of emotional language between the men of all races, past and present. The same emotion, sentiment or passion, *e.g.*, love, jealousy, hatred, vengeance, horror, pity, etc., generally speaking, excites in all similar gestures, similar expression in the features and similar vocalisation and inarticulate cries.

When speech is associated with strong feeling, or an emotion or passion is simulated by the actor or orator, the voice is modulated accordingly in loudness and pitch. The expression of feeling vocalisation is instinctive in the human being as it is in the animal. The growl of the dog is a sign of rising anger and of warning. The vocal expression of anger is to growl; and a curse is usually muttered between the set teeth and is always of a low pitch. But anger beginning in a low tone may end in high-pitched screams. The language of the emotions is, therefore, a universal language; it reveals more truthfully the inmost thoughts and feelings of mankind than articulate language, which is so often employed, as Tallyrand said, "to hide men's thoughts."

In ordinary conversation the medium tones of the vocal register are employed. "The emphatic syllable, however, in a sentence, or that which most strongly expresses the emotional comment on the proposition, is indicated by either the lowest or highest tone of the cadence. And it is interesting to note that it is the oppositeness of choice in this respect that causes the most marked contrast in the Scotch and the English. In English we ascend to the emphatic syllable, but in Scotch we just descend to the emphatic syllable" (Herbert Spencer).

MUSIC AND THE EMOTIONS.

Music arouses in us various emotions, but according to Darwin not the terrible ones of horror, terror and rage. We can see the importance of this fact in the treatment of battle-worn soldiers with terrifying dreams of war by song, which awakens the opposite emotions, such as love, mirth, courage and a *joie de vivre*. Again, music tends to excite rhythmic movements of dancing or marching according to the character of the rhythm. It is an established fact that a band helps greatly in the attack or retreat of a regiment, and songs of soldiers on the march tend to relieve the mind of anxiety and banish the sense of fatigue. Cromwell's invincible Ironsides went into battle singing hymns.

6 THE INFLUENCE OF SONG ON MIND AND BODY,

Music reacts not only on the individual but on the collective or group mind, and its beneficial effects in peace or war become contagious.

Mr. Francis Darwin, in his recent charming essays, tells a little story of the influence of music on our barbaric Saxon ancestors :

“ A Saxon bishop in the seventh century at Sherborne, being unable to attract his congregation to the church, stood on the bridge and played the harp, and thus collected his people, to whom he preached.”

A modern instance of the success of music in attracting people who would otherwise never attend any religious service is afforded by the stirring effect of the Salvation Army Band as it marches through towns and villages, thus collecting the people by its appeal to the emotions and its contagion of enthusiasm, vivifying a religion for those who would otherwise never have come under its influence. Again, history shows that a great patriotic song may have a pronounced vitalising effect on the future of a nation, best exemplified by the “Marseillaise,” which has stirred the souls of millions to fight for victory and liberty. It is sad, but strange, that the great war has not produced in this country any great and noble song. Certainly the Hun produced a remarkable song, “The Hymn of Hate,” which reflected the state of mind of the German people at the time.

ORIGIN OF SONG IN BRITAIN.

The history of song in Britain is of interest, for—

“ Heroic ballads, song and other pieces of our English poets exhibit the customs and opinions of remote ages, of ages which have been almost lost to memory.”—PERCY.

Records show that the Ancient Britons had great respect for their Bards ; and no less respected were the Scalds by the Gothic nations. Moreover our Saxon ancestors, before the introduction of Christianity, as well as the Danes, held men of this profession in greatest reverence. Their skill was considered as something divine ; their persons were deemed sacred ; their attendance was solicited by kings and great nobles, and they were everywhere loaded with honours and rewards. When the Saxons were converted to Christianity, in proportion as letters prevailed among them owing to the influence of the monasteries, the Bards were less and less necessary as historians to sing the deeds and triumphs of kings and nations.

The Bards, therefore, exercised a very powerful influence upon the minds and conduct of the primitive Celtic races of Wales, Brittany and Ireland. As illustrating this may be mentioned the fact that in Wales they formed an organised society with hereditary rights and privileges ; they were treated with great respect and were exempt from taxes and military service. Their musical poems and recitals were handed on from generation to generation solely by memorising, but doubtless each successive bard varied the words and music ; and the same applies to the later minstrels.

FOLK SONG.

Percy remarks how much richer in heroic ballads and songs are the northern counties than the southern. Possibly this may explain the greater appreciation of music and the finer choirs in the north. The folk-song of tradition is the work not of one age but of many, for the songs made by illiterate persons and passed on to others without the aid of printing and writing tended in the course of oral transmission and memorising to lose the traces of individual authority that they may once have possessed. Every country has its own store of folk-songs with national characteristics in idioms, melody and rhythm, distinguishing them from those of other countries.

Mr. Sharpe,⁽²⁾ the leading authority on folk-lore song, has lately visited the Appalachian Mountains, Virginia, U.S.A., inhabited by people of English origin who migrated there in the time of Queen Elizabeth. There are about three million people, isolated from the rest of the world, who have retained the ancient language and customs of the Elizabethan times; they possess a wonderful store of folk songs, which they sing unaccompanied by any musical instrument. They sing these old folk-lore songs while at their work and play, and a large number of them have natural vocal powers of no mean order. The folk-lore songs have been handed down by memory from generation to generation. Naturally numerous slight individual variations have been made in the course of time both in melody, rhythm and words, some of which have been retained, others discarded, by a process of natural selection and survival of the fittest in an unspoiled simple community. This pure folk-lore song is therefore a *communal* and not an individual emotional expression of the mind, and in singing folk-lore song the professional artist is too apt to forget this fact, and while putting his own individuality into his rendering of the song he destroys its communal expression. Mr. Sharpe says the secret of folk-song production is perfect diction and idiom to which melody and rhythm is added; it is the story contained in the folk-song even more than the musical cadence which carries conviction to the audience.

Mr. Baring Gould, Miss Lucy Broadwood, Mr. Keel and Mr. Somerville as well as Mr. Sharpe have collected and arranged many of our old country folk-songs transmitted from one generation to another by memory. Most of these were obtained from *very old men*. Too often our folk-songs have been bowdlerized by hawkers, who, like Autolycus, visit the villages selling their goods, and hearing an old folk-song in the tavern they pick up a part of it, return to London and receive for it a few shillings from a cheap low-class publisher. The song is printed with others on a sheet constituting a "broadsheet," but too often it is not completely remembered and the gaps are filled up in a

debased form. This printed debased form has largely displaced the old folk-song in England.

Song as a musical form falls into two groupings, the one folk-songs, the other art-songs. A line of demarcation between the two cannot be drawn, for there has been action and reaction between them since music began as a cultured art. But folk-song is the natural instinctive inspiration of the human mind, memorised and transmitted, from generation to generation; it constitutes a record of the habits, customs, traditions and aspirations of the common folk, and reflects the individual and collective mentality of the people towards life in all its emotional phases of love and despair, joy and sorrow, mirth and sadness, freedom and oppression, toil and play, victory and defeat.

SONG IN THE ELIZABETHAN PERIOD.

Previous to the Elizabethan period, when our great dramatists and poets blazoned forth, instrumental music as an accompaniment to vocal music both in folk-song and ballads was of the simplest kind. In most of the Shakespearian dramas, also in those of Ben Jonson and Marlowe, there are found stanzas, relics and allusions to these old ballads and poems. Thus—

“ Sigh no more, lady,
Lady, sigh no more;
Men were deceivers ever;
One foot on sea, the other on shore,
To one thing constant never ”

occurs in a very old ballad, “ Holy Friar of Orders Grey ”; and I could cite many other instances, e.g. :

Iago sings a whole stanza from an old Scottish ballad :

“ Tak' thy auld cloak about thee.”

Two stanzas from the Gravedigger's Song in “ Hamlet ” are from “ The Aged Lover Renounceth Love.”

In “ Henry IV,” Act ii, scene 4, Falstaff enters the tavern singing :

“ When Arthur first in Court . . . and was a worthy king.”

This is from an old ballad translated from *Morte D'Arthur* :

The Strolling Minstrels, in Elizabeth's time, had fallen into disrepute, and were classed amongst vagabonds and vagrants, and liable to be imprisoned as such. An old ballad, “ A Song of the Lute ”:

“ When griping's griefs the heart would wounde,
And doleful dumps the mind oppress,
There Music with her silver sound
With spede is wont to send redress,
Of troubled minds for every sore
Sweet music hath a salve in store.”

In "Romeo and Juliet" Shakespeare makes Mercutio ridicule "Music with her silver sound" as being more the sound of the silver which interested the musicians more than the music.

Doubtless Shakespeare knew that these old ballads were deeply impressed in the minds of the people, and that their introduction would add greatly to the popularity of his plays.

LYRIC SONG.

The polished products of culture and art in lyric song reached their zenith with Schubert, that great musical genius, who at eighteen wrote the "Erlkönig." It is remarkable enough that with little education and opportunity he should have composed such rare and beautiful music; but it is even more wonderful that he should have shown such insight into the emotions and passions of the poems to which he set the music. He composed his music to many of Heine's poems, which are very nearly impossible to translate, because the poem and the music are in perfect association and each supreme in expression of the emotions. In "Who is Sylvia?" the English words of Shakespeare are in perfect association with the musical cadence because there is the complete harmony and beauty of expression of the two great masters. Schubert had also that qualification which many song-writers do not possess, *viz.*, a knowledge of the human voice, its powers and limitations, which was partly intuitive, partly the result of his experience as a chorister.

Great musical geniuses, like great poets, are born, not made, and a perfect sense of musical cadence cannot be acquired by individuals possessing only an infinite capacity for taking pains.

As the expression of the emotions and passions by the appreciation and production of variations of pitch and rhythm in the human mind was probably the forerunner and origin of articulate language, music is therefore more stably organised in the brain and develops instinctively at an early age, and in some individuals to an extraordinary degree of perfection. Only in this way can we explain the number of extraordinary prodigies of musical genius, of whom Schubert, Mozart and Richard Strauss are outstanding examples. For the same reason an intuitive mode of expressing feelings and passions by modulation of the voice is common to all human beings, and because instinctive, it is more truthful than is articulate speech.

THE QUALITY OF THE VOICE INHERITED.

The quality of the voice depends upon the shape and condition of the resonators, which add the overtones to the sound produced by the vibration of the vocal cords.

Now it is an interesting fact, pointed out by Francis Galton, that the

quality of the voice depends upon inherited conditions, whereas articulate expression and handwriting do not ; these are acquired by imitation. When we consider that the physiognomical characters of an individual very largely depend upon the shape of the nose and nasal passages with the other hollow cavities in the mask of the face, which form (together with the mouth and throat) the resonators of the human voice, and give to it the peculiar personal qualities which distinguish it from other voices, it is easily understood that just as the features and neck of our ancestors may be handed down from generation to generation (*e.g.*, the Bourbon nose and the Hapsburg lip for 500 years), so the quality of the voice (which, as we have seen, is so intimately dependent upon structures which are associated with physiognomical characters) is handed on from generation to generation. This proves how true is the statement of the old Roman poet and philosopher, Lucretius: "Sometimes, too, the children may spring up like the grandfathers and often resemble the forms of their grandfathers' fathers, and repeat not only the features but the voice and hair of forefathers."

VOICE PRODUCTION IN SINGING AS A GENERAL HYGIENIC MEASURE.

The art of singing consists in the control of the breath and the proper management of its mode of escape through the glottis, mouth and nose.

The teaching of singing, by inculcating the habit of breathing through the nose and fully expanding the lungs, should therefore serve as a health restorative in convalescent lung cases, whether arising from disease or "gassing." Moreover, singing, by producing an individual and collective sense of joy and well-being, promotes digestion, assimilation and nutrition, thereby aiding convalescence of all forms of mental and bodily disease.

The nasal passages are so constructed as not only to serve the sense of smell but to warm and filter the inspired air. The nose thus acts as Nature's sentinel to the respiratory passages. Instruction in singing, by establishing a habit of breathing through the nose, serves therefore as a means of diminishing the liability to acute and chronic catarrhal affections of the bronchial tubes and lungs caused by the entrance of irritant particles, germs of disease and cold air.

" In sweet music is such art
Killing care and grief of heart,
Fall asleep or hearing die."

HENRY VIII, Act iii. Sc. 1.

Inasmuch as music is associated with pleasure and the nobler feelings and passions of love, tenderness, joy, mirth, the martial spirit and rhythmic dance, rather than with pain, fear, terror, grief, horror, anger and rage, it tends to initiate and energise the former and drive

away the latter. These latter emotions and passions are associated with particular changes in the bodily state, *viz.*, the quickening or slowing of the pulse and respiration, the emotional thrill or shudder of the spine, pallor and coldness or redness and warmth of the skin, with dilatation of the pupils, etc. Not only are there these changes in personality of which we are conscious by bodily feelings, but associated therewith are subtle bio-chemical changes in the blood caused by an increased production and outpour of adrenalin, which plays an all-important part in the defensive mechanism of fright and fight.

SINGING FROM AN EDUCATIONAL STANDPOINT.

"Great is song used to great ends."—TENNYSON.

Although the greater number of disabled and invalid soldiers are not capable of doing more than sing in choruses and part songs, and the singing teacher (from a high artistic point of view) may find teaching them a humble occupation, yet according to my experience at the Maudsley Neurological Clearing Hospital, it will certainly not be a barren one, for it will bring joy into their lives and help them to forget the terrible experiences they have passed through. Moreover, it will fill their minds with a store of fine melodies. But among these soldiers the singing teacher will occasionally find good musicians and solo singers anxious to improve their voice production.

(²) At a meeting of the Society of English Singers, Mr. Sharpe gave a charming account of this visit and some of his experiences.

4. HISTOLOGICAL EXAMINATION OF THE BRAINS OF ANIMALS EXPOSED TO THE GAMMA RAYS OF RADIUM

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MATERIAL AND METHODS OF INVESTIGATION.

The brains of 57 animals were sent including normal. These animals were frogs, rats, rabbits, and cats. In some cases the brains were fixed in formol saline and some in 96 per cent. alcohol. Of these 57 animals observations on 30 are recorded.

The methods employed for investigating the material were as follows. The tissues were blocked in paraffin and sections of 10μ made. These were stained by Nissl, toluidin blue and eosin for the cells and Mann's method for eosinophil reactions. Ranke's Victoria blue method for glia and Van Gieson for general reactions. Frozen sections were also made from formalin hardened material for lipoid granules.

Most of the animals were killed by breaking the neck or cutting the carotid arteries; some died a natural death during the exposure or after some days following the experiments. Two sent that were killed by chloroform were rejected as unsuitable. No definite information regarding nervous trouble having arisen during or after the experiment was furnished. This had its advantages and disadvantages. On the one hand, had nervous trouble been noticed, an intensive investigation of one part of the brain might have been made and not of the rest. Undue significance might have been attached to changes in consequence. On the other hand, where there was *definite* and *reliable* change found it would have been of interest to have noted symptoms that could have been correlated with the same, e.g. the changes in the Purkinje cells. Still in these small animals it is extremely difficult to distinguish symptoms due to organic changes from those due to the nervous condition produced by the unfamiliar

surroundings in which they find themselves. Thus it would be extremely difficult to investigate nystagmus, ataxia or atonia in the limbs of the animal.

The changes observed were varying degrees of alteration or disappearance of the chromophilous basophile substance of the cytoplasm and some nuclear changes, but in these instances, where the length of time exposure was short, there was little difference from those observable in the brains of small normal animals.

RESULTS OF MICROSCOPIC EXAMINATION.

RAT (1).

48 hours' exposure to 5 gms. Ra Br₂, 2 H₂O.—death 2 days later.

Cortex. Few cells retain their pyramidal shape and show hyperchromatosis. A great majority of cells show swelling, have lost their pyramidal shape and the processes are indistinctly seen—especially their apical process. The nucleus is swollen and often eccentric. (Fig. 2.) This statement applies to all the different layers of pyramids and polymorphs. Exactly the same applies to the cortex of the neo- and archi-pallium. Examined with an oil immersion marked nuclear change is very apparent. The nucleus is so much swollen as to occupy nearly the whole of the body of the cell. The nuclear membrane is infolded and in the middle of the nucleus is seen the dark purple staining nucleolus. A number of small vacuoles is seen within the nucleus. The cytoplasm is almost devoid of basophile substance and consists of a network with only a thin incrustation of dust-like basophile substance.

Base of Brain. Cells show less marked changes.

Choroid Plexus. Cytoplasm of cells greatly diminished, nucleus swollen and deeply stained. Differentiation between nucleus and cytoplasm very indistinct.

Cerebellum. Layer of granules fairly well stained. Under low power the Purkinje cells appear to be well stained. Examined with an oil immersion it is seen that the chromophilous substance in some of the cells is on one side in the shape of a crescent; in others the cells are diffusely stained a deep blue.

Large Cells in the Pons. The nucleus in many of the cells is swollen, the outline is irregular and merging into the trabecular network of the cytoplasm; the nucleolus is very distinctly stained. The Nissl granules are not seen, only a fine dust of chromatin substance appearing on a network. Examined by an oil immersion these cells show no definite nuclear membrane, the nucleolus deeply stained and around is a dull purple irregular stained substance; and surrounding this is an irregular space with fine threads traversing it and merging into the cytoplasm. This appearance is different to an ordinary peri-nuclear chromatolysis and is indicative of a physical as well as a chemical change. In some of the cells the nucleus appears to have been destroyed; in none can the nuclear membrane be distinctly seen. This description applies to an average condition of the cells; in other parts the cells show more advanced change, in others less, but nowhere can normal cells be discovered. (Figs. 1 and 2.)

RAT (2).

Exposure of 46 hours—killed.

Cortex. Under low power magnification the cells show less swelling and are better stained than those in Rat 1. It is quite obvious that there is a marked change in all the cells both in the neo- and archi-pallium. In the archi-pallium many of the cells show the basophile substance accumulated at one end of the cell.

Pons. Practically the same condition as Rat 1 except that the change is not so marked and there is a little more basophile substance in some of the cells.

Cerebellum. Cells of Purkinje show in some instances hyperchromatosis and shrinkage, others show an accumulation of basophile substance on one side, while others show a complete disappearance of basophile substance.

RAT (3).

24 hours' exposure—died 2 days later.

Cerebellum. The Purkinje cells show accumulation of basophile substance like a cap or a crescent at one side of the cells. The rest of the cell, especially opposite side to the crescent, is more or less disintegrated. The nucleus is stained a dull blue with nucleolus stained a deeper colour. The nuclear membrane, when it can be seen, is infolded, and there is obviously marked change in the nucleus as well as in the cytoplasm of the cell. Not a single normal Purkinje cell can be seen and no processes are visible. The granular layer appears rather faintly stained, but not much morphological change is observable. (Figs. 3 and 25.)

Pons. The cells show similar appearances to those described in 1 and 2. Some of the cells appear to be entirely destroyed, nucleus extruded, in others the nucleus is on the surface and on the point of being extruded. The nuclear membrane is either not visible or very irregular in outline or swollen. (Figs. 4 and 27.)

RAT (4).

12 hours' exposure—killed.

Pons. Under low power magnification the cells show apparently little change and the outline of cells is more normal in appearance, especially does this apply to multipolars. The large cells, some of which as in microphotograph, show apparently fairly normal pattern of Nissl bodies and normal nucleus. In others, however, the Nissl bodies are not so distinctly seen and there is a tendency to hyperchromatosis; in the immediate neighbourhood are large pontine cells which show commencing chromatolysis and disintegration of cytoplasm. The only cells which might pass for normal are the very large cells figured in photomicrograph no. 5, but these are relatively few. However, when examined under oil immersion, the apparently normal cells are seen to show marked changes. The Nissl granules are broken up into a fine dust, for the most part there are no Nissl granules on the processes; the nucleus is swollen and clear, with an irregular outline, in fact there is a very considerable early change.

Cerebellum. Purkinje cells are the same as the other cases, but there is not quite so marked a directional change. (Fig. 6.)

RAT (5).

12 hours' exposure—died 2 days later.

Cerebellum. Purkinje cells show similar changes as in the other rats only the crescent is even more marked. (Fig. 7.)

Pons. The changes in the large cells appear to be more marked. The nucleus is not visible in most of these large cells and there is a marked chromatolysis. (Figs. 8 and 28.)

RAT (6).

24 hours' exposure—killed.

Cerebellum. The granules are less stained than the Purkinje cells, which is not usual. Many of the Purkinje cells show disintegration on one side of cell, with feeble staining and accumulation of basophile substance, but this is not so definitely directional as in other cases.

Pons. The cells have more normal appearances as regards shape and processes, but examined with oil immersion it is seen that they are uniformly stained a dull purple and the Nissl granules are not evident.

Cortex. Obviously marked change in cortical cells but pyramidal shape retained better than in Rat 3. Most of the cells show some nuclear and cytoplasm change as in Rat 3.

RAT (7).

Exposure 6 hours—killed.

Cerebellum. Low power, layer of granules faintly stained. Purkinje cells deeply stained, 'hyperchromatosis'. No definite evidence of crescent cap, whole cell stained a deep blue, nucleus quite distinct, processes not seen. Examined with an oil immersion the layer of granules appears swollen and very pale. Purkinje cells are oval in shape, very occasional process seen. In many cells no difference of nucleus from cytoplasm, in others only indistinctly seen. When nucleus is seen it is irregular in outline and nucleolus hardly visible, being of same stain as rest of nucleus.

Choroid Plexus. Choroid plexus quite empty of blood, epithelium appears shrunken and stained almost a uniform blue without any nuclear differentiation.

Pons. There are only a few of the motor cells which retain more or less their shape and processes; and these show a hyperchromatosis; they are scattered among cells which are more obviously changed morphologically. The greater number of cells have a large pale nucleus, the nucleolus not taking the basophile stain properly and the cytoplasm consists of an irregular network faintly incrustated with fine basophile stained dust. Many of the smaller cells appear to be disintegrated, leaving only the pale nucleus behind. There is no regularity in the disposition of the affected and slightly affected cells.

(This morphological change corresponds to what one finds in experimental anaemia). The small cells seem to be very markedly affected.

RAT (11).

Exposure 16 hours—killed.

Cortex. The surface of brain was covered with blood corpuscles (probably due to mode of death). Under a low power the cells show a more normal appearance in shape and presence of Nissl granules, but even the larger cells and all the smaller cells show some chromatolysis, but there is not the same degree of abnormal appearances observed in the other cases.

RAT (12).

16 hours' exposure—killed 48 hours later.

Cerebellum. The Purkinje cells do not show definitely the 'cap' as observed in some of the other cases. The nucleus is swollen and irregular in outline in many of the cells. The cytoplasm shows a purple diffuse dust incrusting the network. The granular layer is comparatively poorly stained.

Pons. The large multipolar cells show marked changes, viz. swelling of cell; breaking off of processes; absence of Nissl granules and a network in the cytoplasm incrustated with basophile dust. Some of the multipolar cells retain their shape and processes, but do not exhibit normal Nissl granules and have a tendency to hyperchromatosis. The change in the cells has no regular group disposition.

RAT (13).

3 hours' exposure and killed immediately after.

Pons. Examined with a low power the large multipolar cells exhibit Nissl granules, but these do not appear quite normal, an early chromatolytic change is visible. (Fig 9.)

Examined with an oil immersion, nuclear changes are seen, and a majority of cells do not show normal Nissl granules. The processes are broken off, there is a distinct diminution of basophile substance and the cytoplasm consists of a network incrustated with fine dust of basophile substance with here and there remnants of Nissl bodies. (Figs. 9 and 26.) The small cells show more considerable changes of the same nature. (Fig. 9.)

Cerebellum. The layer of granules is better stained but not so well as normal. Purkinje cells show swelling of the nucleus, irregular outline, absence of Nissl bodies, processes not seen, no 'cap' but tendency for basophile substance to clump. (Fig. 10.) Examined with an oil immersion there is evidence in some of the cells of directional change.

RAT (14).

3 hours' exposure—killed 3 days after exposure.

Pons. Under a low power magnification the large multipolar cells seem less affected than in Rat 13, as though some recovery had taken place (Fig. 11), but under an oil immersion there is evidence of considerable chromatolytic change in the great majority of the cells indicating that they would not recover. Some of the cells are covered with satellite cells.

Cerebellum. Under a low power magnification the Purkinje cells are not all equally stained, some are swollen and round as in Rat 13, others seem to retain their shape and the stain. (Fig. 12.) Examined with an oil immersion most of the cells are swollen and show swelling of the nucleus, breaking off and absence of processes and irregular network incrustated with basophile dust, but some are not swollen and retain their shape and are fairly well stained.

RAT (16).

3 hours' exposure, killed 9 days after exposure.

Not much difference to normal.

RAT (18).

3 hours' exposure and allowed to live 3 days before killing.

Cortex. Slight chromatolytic change.

Pons. No very marked change.

RAT (19).

Exposure 3 hours and killed immediately after exposure.

RAT (20).

3 hours' exposure and killed 4 days later.

No definite change.

RAT (22).

3 hours' exposure and killed 9 days later.

No definite change.

RAT (23).

Exposure of 5 minutes weekly for 12 course weeks.

Nothing of note.

NORMAL RATS.

Pons. Cells show condition very similar to those which have been described in animals with short exposures, but there is this marked difference, for groups of multipolar cells can be seen with normal tigroid pattern of Nissl granules. But the normal rat shows breaking up of the Nissl granules into a fine dust in the large cells.

This indicates that only the more marked changes observed in the multipolar cells of rats exposed to radium can with certainty be associated with the effects of the emanations.

CAT A.

Exposure 24 + 24 + 24 + 16 + 16 = 104 hours: died during last exposure.

Pons. Large multipolar cells show considerable chromatolysis and absence of the tigroid pattern of the Nissl granules. The nucleus has an irregular outline swollen and elongated in the long axis of cell. In the cytoplasm there are numbers of empty unstained spaces, rest of cell stained a diffuse blue. Condition might be the result of exhaustion. (Fig. 13 does not show much change, but when examined with oil immersion appearances are as in Fig. 31.) Compare with Fig. 33 (Normal Cat).

Cerebellum. Similar appearances in cells of Purkinje, swelling of nucleus, indefinite outline merging into vacuolated cytoplasm. The basophile substance appears to be more marked on one side of the cell; it does not, however, form such a definite crescent as in the case of the rat. The layer of granules is faintly stained. (Fig. 14.)

CAT B.

Exposure 24 hours 10.2.20, 12 hours 13.2.20.

Pons. The pons shows the same appearance as Cat A except that the Nissl granules are to be seen, but there is the same vacuolation, swelling of nucleus and indistinct nuclear membrane. (Fig. 15.)

CAT D.

Exposure 6 hours flush to flank, 13.2.20, 24 at 15 cm. 29.6.20, died 12.7.20.

Pons. Large multipolar cells normal shape, Nissl granules seen, nucleus present but deficiency of basophile substance as shown by very light staining. (Fig. 16.)

Cortex. The pyramidal cells poorly stained in deeper layers, broken up, and many of them show numbers of satellite cells around. (Fig. 17.)

CAT E.

Exposure 16 hours at 15 cm. 19.2.20; 41 hours at 15 cm. 20.2.20; 20 hours at 15 cm. 23.2.20; 18 hours at 15 cm. 24.2.20. Total exposure 95 hours: died 29.2.20.

Pons. Some chromatolysis of cells, swelling of nucleus and vacuolation of cytoplasm. (Figs. 18 and 30.) The large multipolar cells seem to be somewhat shrunken and many exhibit no Nissl bodies, but a diffuse stain and vacuoles. Some of the cells show Nissl bodies as seen in Fig. 18.

Cortex. Examined with an oil immersion the Betz cells show hyperchromatosis and the Nissl granules are abundant. The pyramidal cells show a vacuolation of cytoplasm, absence of Nissl granules and swelling of nucleus. The apical processes are indistinctly seen; it is difficult to state how far these conditions are due to pathological process directly caused by the emanations of the radium. (Fig. 19.)

RABBIT 2.

Exposure 16 hours at 15 cm. 1.4.20: killed 7.4.20.

Pons. Considerable chromatolysis and disappearance of Nissl granules; with vacuolation of cytoplasm. Large swollen nucleus with irregular outline and perinuclear chromatolysis. Some of the cells exhibit a normal outline, nucleus not increased in size but distinctly seen, nucleolus deep blue and Nissl granules indistinctly seen. (Fig. 20.)

Cortex. Pyramidal cells for the most part retain their shape and columnar arrangement, the apical process can be seen; they all show a diffuse colouration of the cytoplasm with vacuolation and absence of Nissl granules. (Fig. 21.) The nucleus in many cells is swollen and irregular in outline.

Cerebellum. The Purkinje cells show a considerable degree of chromatolysis. No Nissl granules are observable. Some cells are almost devoid of basophile substance. A few cells show hyperchromatin at one pole. The granule layer is poorly stained as a whole.

RABBIT 4.

Exposure of 16 hours at 15 cm., 6.4.20., killed immediately after exposure.

Pons. Many of the large multipolar cells are apparently disorganized and show no Nissl bodies, and the cytoplasm is either vacuolated or disintegrated. The nucleus in some of the cells cannot be seen; this may be due to its having become eccentric. (Figs. 22 and 32.)

RABBIT 8.

24 hours' exposure—killed 9 days later.

Pons. Multipolar cells show the same appearances, irregular outline of nucleus and swelling, Nissl granules not clearly seen, vacuolation and diffuse staining in cytoplasm.

RABBIT 10.

3 exposures of 16 hours each on 3 consecutive days—killed immediately.

Pons. Multipolar cells show more marked chromatolysis and Nissl bodies less evident than in Rabbit 11. Nuclear changes similar but more obvious; some of the cells show almost complete absence of basophile substance. (Fig. 23.)

RABBIT 11.

3 exposures of 16 hours each on 3 consecutive days—killed immediately.

Pons. Large multipolar cells have a normal Nissl pattern, rather faintly stained blue but not quite so brilliant a colour as normal. Nucleus network can be seen; outline of nuclear membrane normal. This applies to one large cell (Fig. 24), but other cells in same group are not quite so normal in appearance, for the Nissl granules are beginning to break up. The outline of the nucleus is indefinite and irregular and merging into colourless space of cytoplasm. Some of these cells look shrunken. Many of the smaller cells are more markedly affected than the larger ones. (Fig. 29.)

RABBIT 15.

3 exposures of 16 hours at 15 cm.—killed on 7th day after exposure.

Pons. Under low power the shape of the multipolar cells appear to be normal, with nucleus in middle of cell.

Under oil immersion Nissl granules broken up in a great many of the cells and nucleus swollen. Just as marked a change in this rabbit as in numbers 10 and 11.

SUMMARY OF OBSERVATIONS.

Rats.

The histological changes in the brains of the rats are the most pronounced. There is a certain degree of correspondence in the histological changes and the length of time of exposure, although there is no definite relationship. On the one hand it seemed that an animal which had been subjected to a *short term* of exposure and allowed to live some days exhibited less alteration in the cells than an animal exposed for the same time and killed immediately after the experiment had ceased. From this it may possibly be inferred that recovery was taking place (*vide* Rats 13, 14, and Figs. 9, 10, 11, 12, and 26). On the other hand, animals which had been exposed for *long periods*, e.g. 12 hours, and died 2 to 3 days later, showed more marked cell changes than an animal with a corresponding time exposure and killed immediately after the experiment (*vide* Rats 4 and 5, Figs. 5, 6, 7, 8, and 28). The most obvious change which can be associated with the effects of exposure to the radium was observed in the Purkinje cells of the cerebellum; a change not previously described, so far as we are aware, and therefore it may be assumed that it is directly due to the effects of prolonged exposure to the radium.

It was not observed in the cerebellum of rats with an exposure less than 12 hours. No definite evidence of a directional change was observed after 6 hours' exposure (*vide* Rat 7). There was not always a constant relationship between the degree of directional change and the length of time of exposure. In Rats 3, 4, and 5, the Purkinje cells show a crescent of basophile substance on one and the same side (*vide* Rats 1, 3, 4, 5; Figs. 3, 6, 7, and 25).

After these results had been observed it was ascertained that the rats had been fixed in such a position that the side of the brain had been exposed to the direct beam of the rays, and this may account for the fact that the basophile substance has been displaced in these large cells in the characteristic manner shown.

Cats.

It may be stated generally that compared with the rats the cell changes observed were slight and inconsiderable, even after very long exposure, e.g. 41 hours and after a succession of long exposures totalling respectively 95 and 104 hours (*vide* description, Cats A and B). The changes in the cells can only be definitely ascertained by examination with an oil immersion lens (*vide* Figs. 13, 14, 15, and 31).

Two animals lived some time after the exposure, Cats D and E (*vide* Figs. 16, 17, 18, and 19).

In Cat D the only characteristic change of importance is the large number of satellite cells seen around the poorly stained pyramidal cells of the cortex. It is probable that this change is indicative of a low state of vitality of these cells. Satellite cells were not seen in other cases as a rule. Possibly this may be due to the long period of time elapsing after the exposure and the effects on the general condition of the animal and its other organs.

Very little definite inference can be drawn from the observations in the brain of Cat 1; although as Fig. 19 shows there is some evidence of hyperchromatosis of one part of the cells possibly of a directional nature.

Rabbits.

The Purkinje cells of the cerebellum show marked chromatolysis but no definite evidence of a directional change as seen in the rat's brain. The chromatolytic changes in the cells of the brain of the rabbit, although the duration of exposure was less, are more marked than in the cat (*vide* Figures 20, 21, and 29, and descriptions of rabbit 2, also Figures 22, 23, 24, and 32, and descriptions of rabbits 8, 10, 11, 15).

GENERAL CONCLUSIONS.

The general and practical conclusions arrived at from these observations and from the fact that no gross nervous symptoms were reported even in animals that had lived days, weeks or

months after exposure, is that the central nervous system does not suffer to any great extent in the larger animals such as cats, even after prolonged exposure to 5 grammes of radium. This may be due to the thicker protective coverings of the brain in these animals.

We desire to express our obligations to Mr. C. Geary for valuable assistance in the work, both as regards observation and the preparation of the sections and photomicrographs.

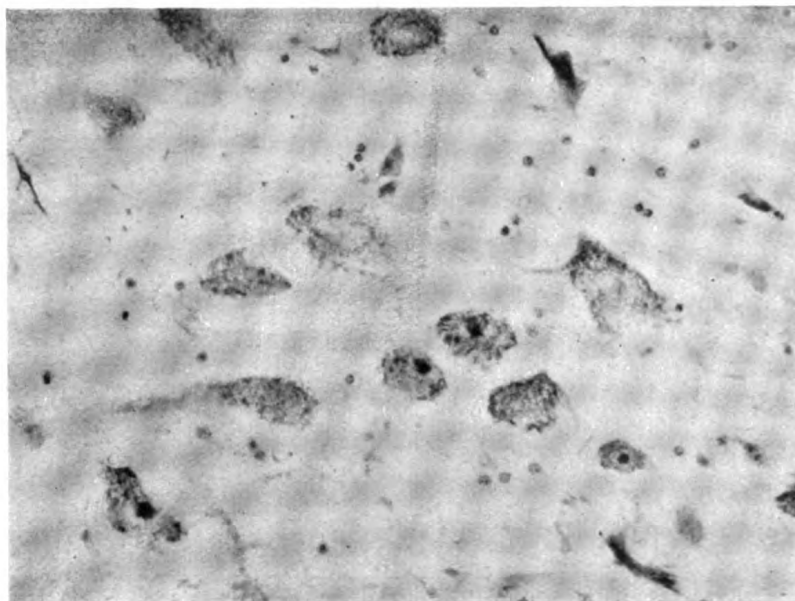


FIG. 1. Rat, No. 1. Exposed to 5 gm. of radium bromide for 48 hours ;
died 2 days later. Section of pons. $\times 400$.

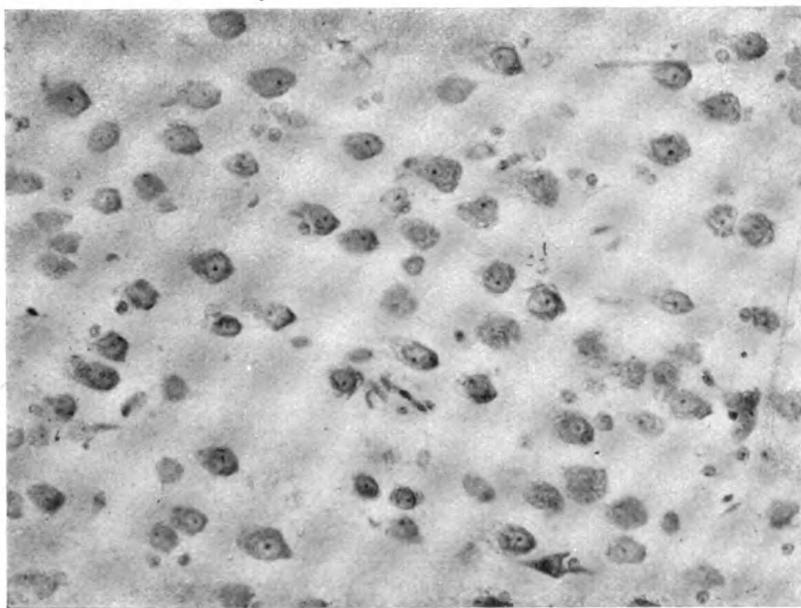


FIG. 2. Rat, No. 1. Section of cortex. $\times 400$.

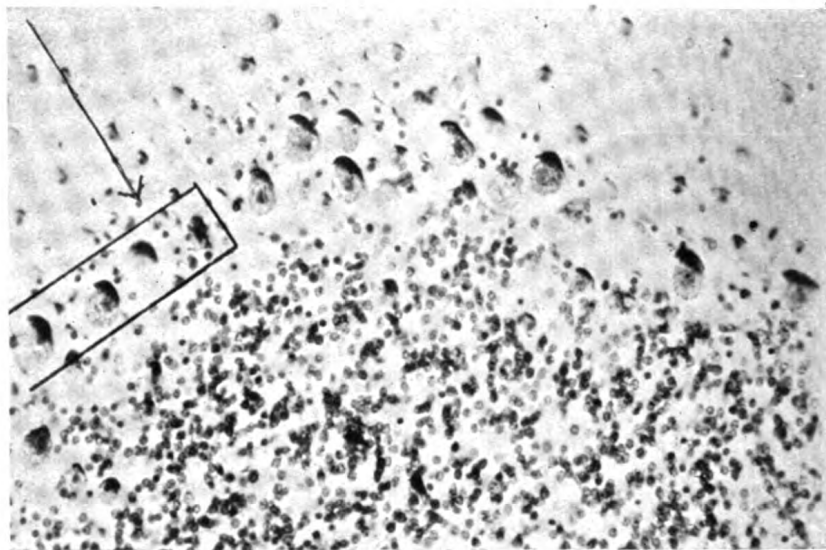


FIG. 3. Rat, No. 3. Exposed to 5 gm. of radium bromide for 24 hours; died 2 days later. Section of cerebellum. $\times 400$. The four cells marked are shown on a larger scale in the colour drawing (Fig. 25).

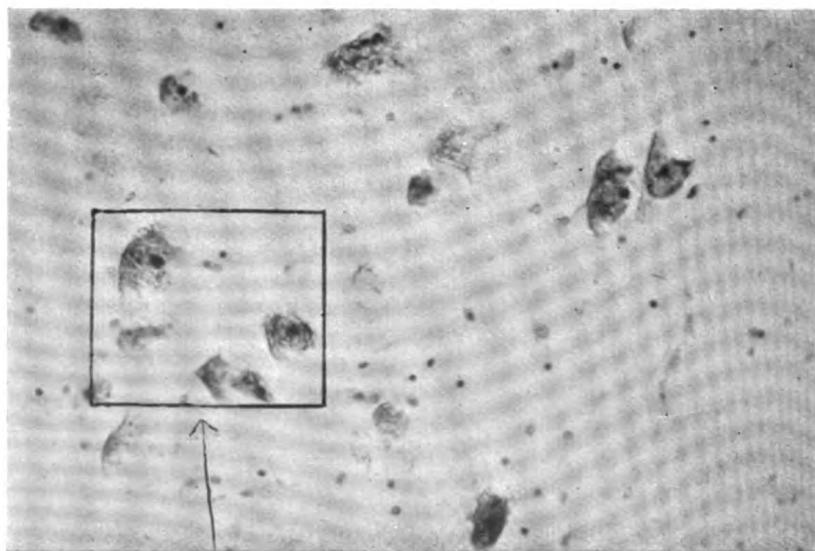


FIG. 4. Rat, No. 3. Section of pons. $\times 400$. The four cells marked are shown in Fig. 27.

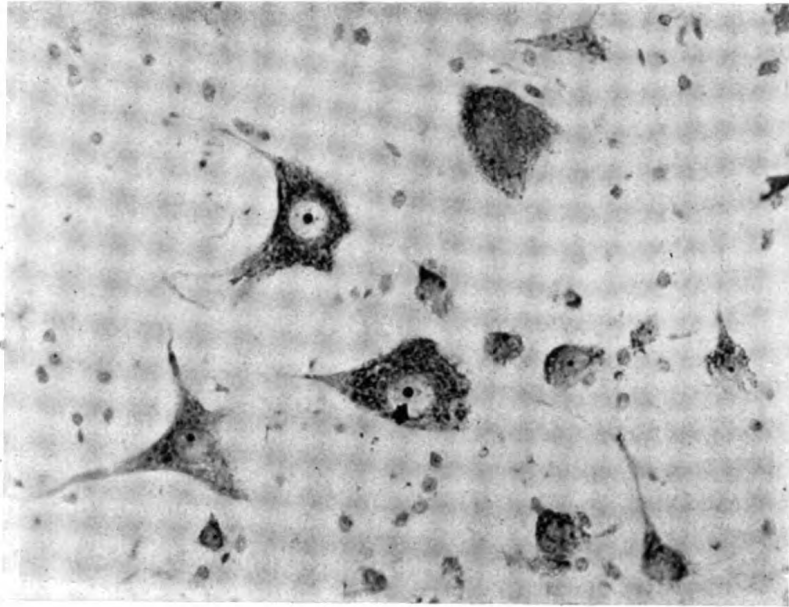


FIG. 5. Rat, No. 4. Exposed to 5 gm. of radium bromide for 12 hours ; killed immediately after. Section of pons. $\times 400$.



FIG. 6. Rat, No. 4. Section of cerebellum. $\times 400$.

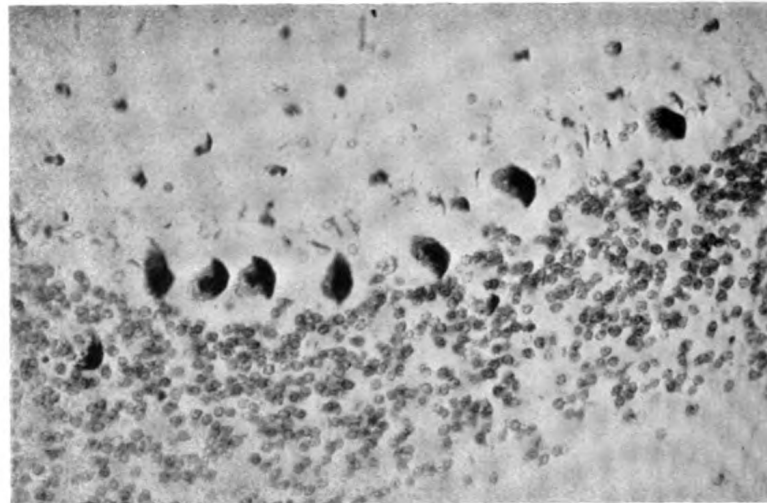


FIG. 7. Rat, No. 5. Exposed to 5 gm. of radium bromide for 12 hours, 8/10/19; died during night 10-11/10/19. Section of cerebellum. $\times 400$.

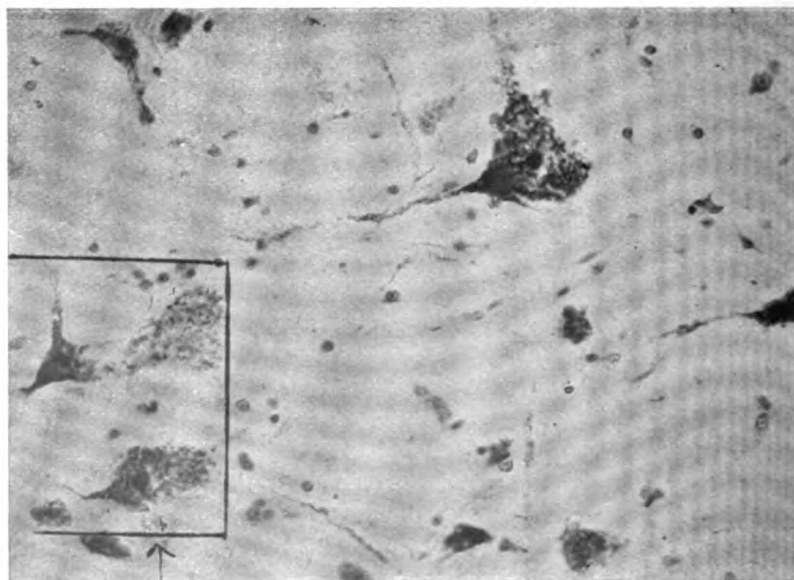


FIG. 8. Rat, No. 5. Section of pons. $\times 400$. The three cells marked are shown in Fig. 28.

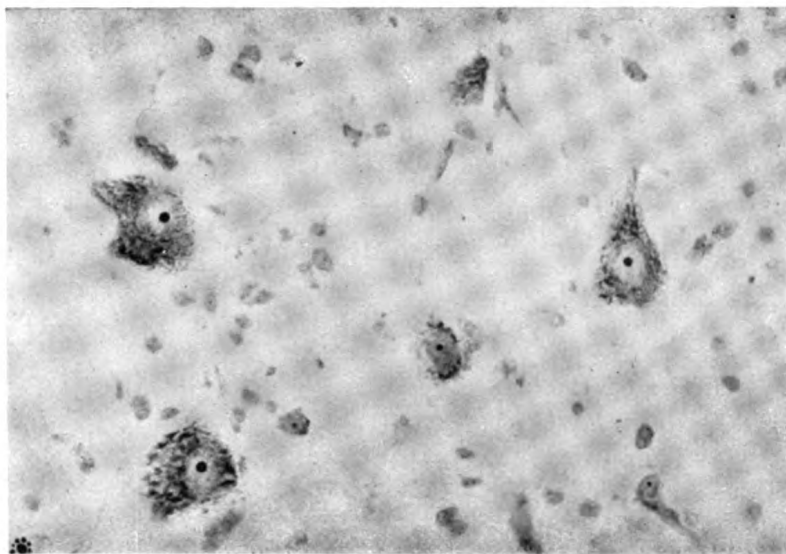


FIG. 9. Rat, No. 13. Exposed to 5 gm. of radium bromide for 3 hours ; killed immediately after. Section of pons. $\times 400$.

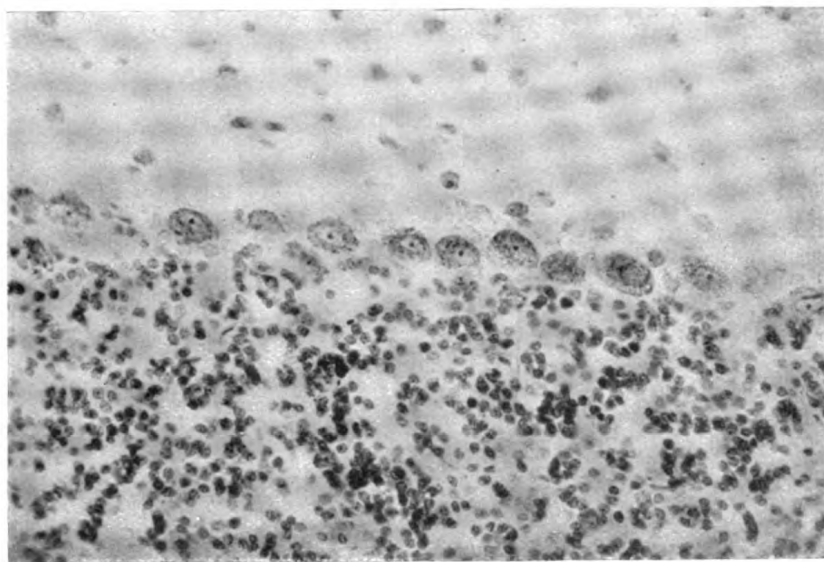


FIG. 10. Rat, No. 13. Section of cere'ellum. $\times 400$.

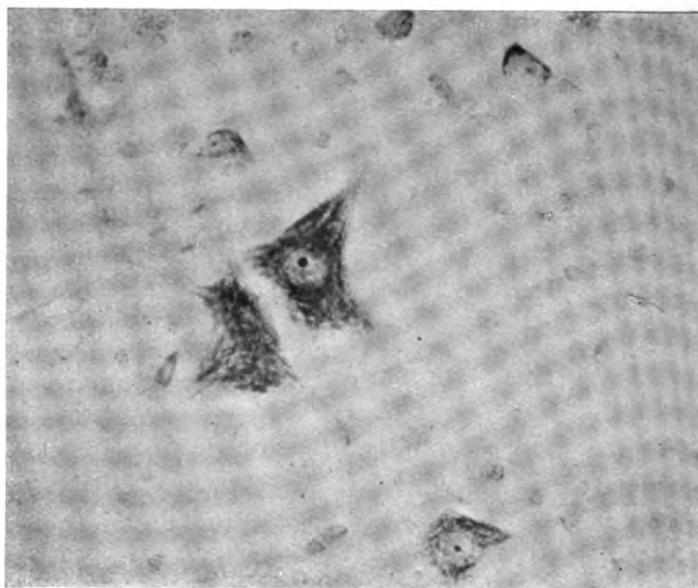


FIG. 11. Rat, No. 14. Exposed to 5 gm. of radium bromide for 3 hours; killed 3 days later. Section of pons. $\times 400$.

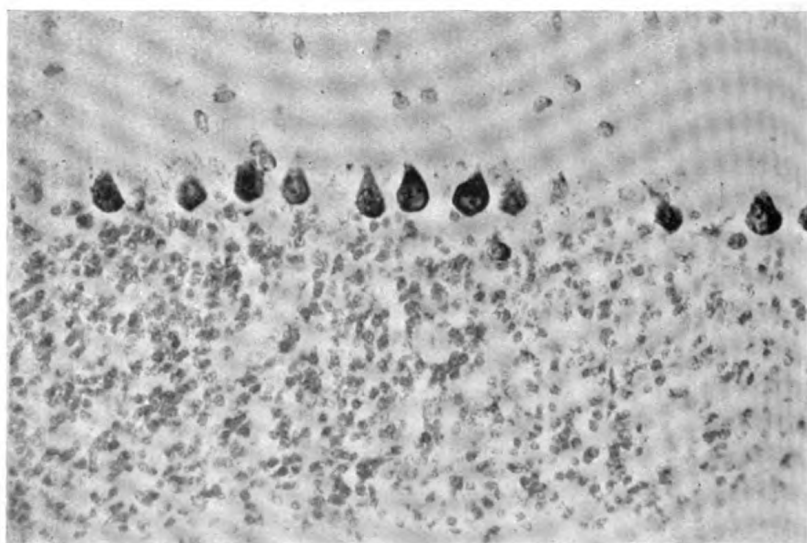


FIG. 12. Rat, No. 14. Section of cerebellum. $\times 400$.

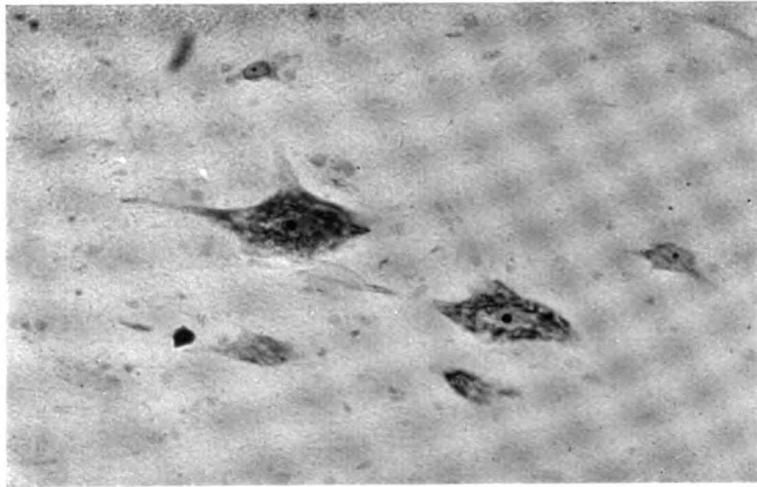


FIG. 13. Cat A. Exposed for $24 + 24 + 24 + 16 + 16 = 104$ hours; died during last exposure. Section of pons. $\times 400$. See also Fig. 31.

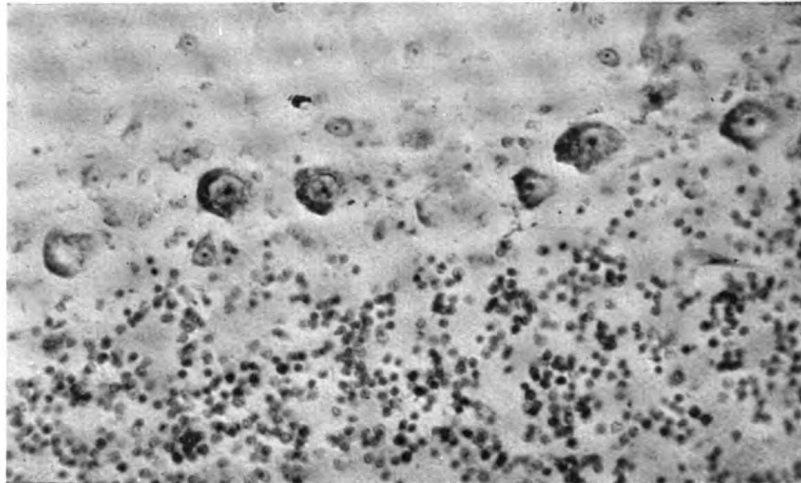


FIG. 14 Cat A. Section of cerebellum. $\times 400$.

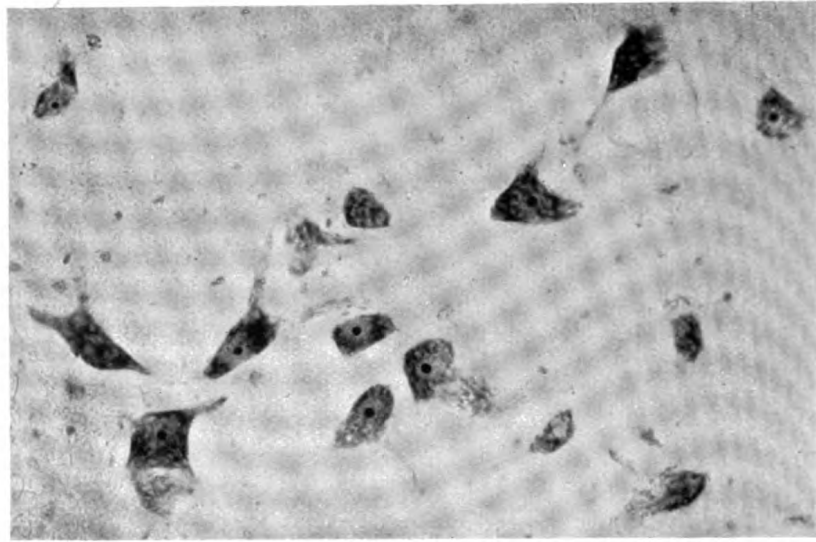


FIG. 15. Cat B. Exposed for 24 hours 10/2/20 and for 12 hours 13/2/20. Section of pons. $\times 400$.

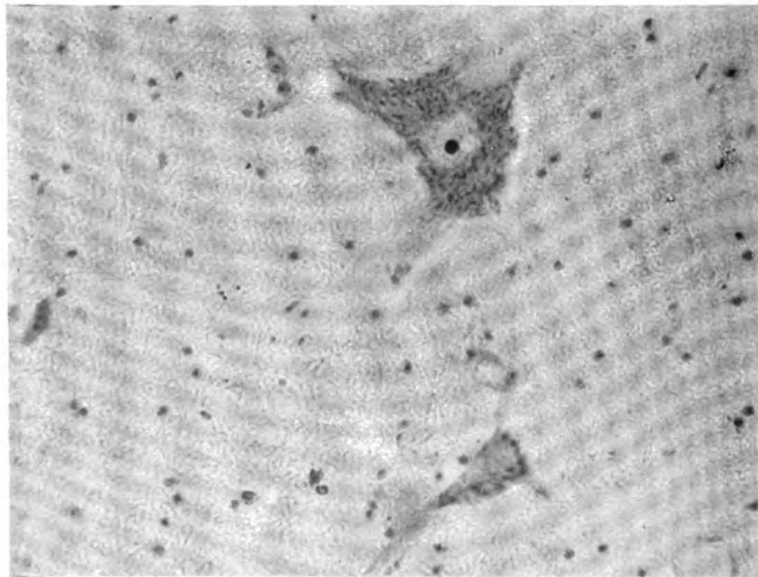


FIG. 16. Cat D. Exposed for 6 hours flush to flank 13/2/20 and for 24 hours at 15 cm. 29/6/20; died 12/7/20. Section of pons. $\times 400$.

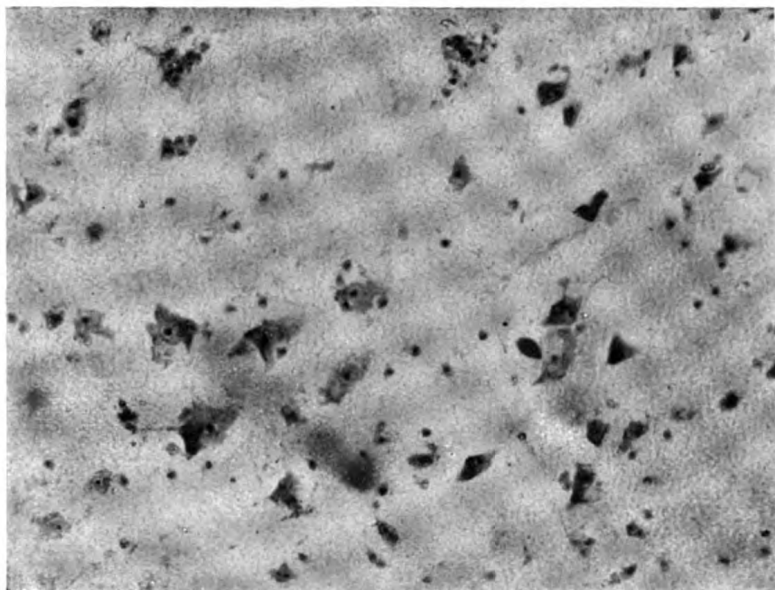


FIG. 17. Cat D. Section of cortex. $\times 400$.

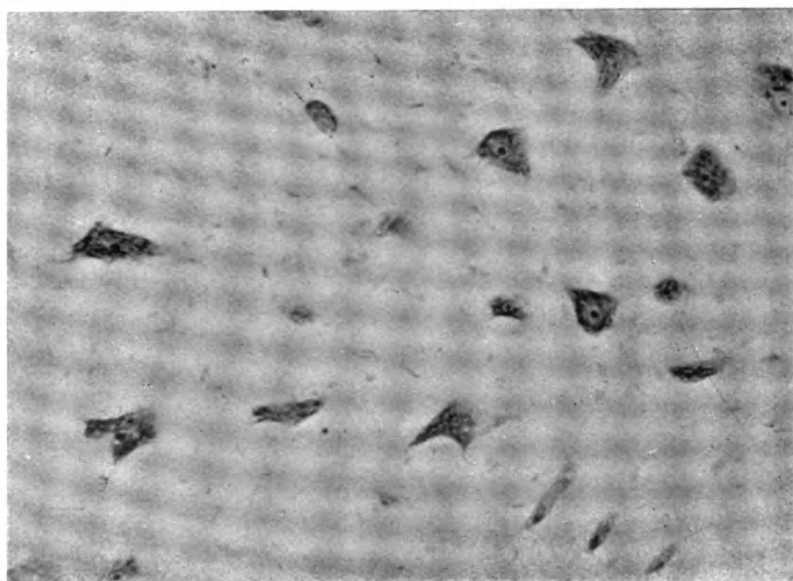


Fig. 18. Cat E. Exposed for 16 hours at 15 cm. 19/2/20; for 41 hours at 15 cm. 20-22/2/20; for 20 hours at 15 cm. 23/2/20, for 18 hours at 15 cm. 24/2/20; died 29/2/20. Section of pons. $\times 400$.

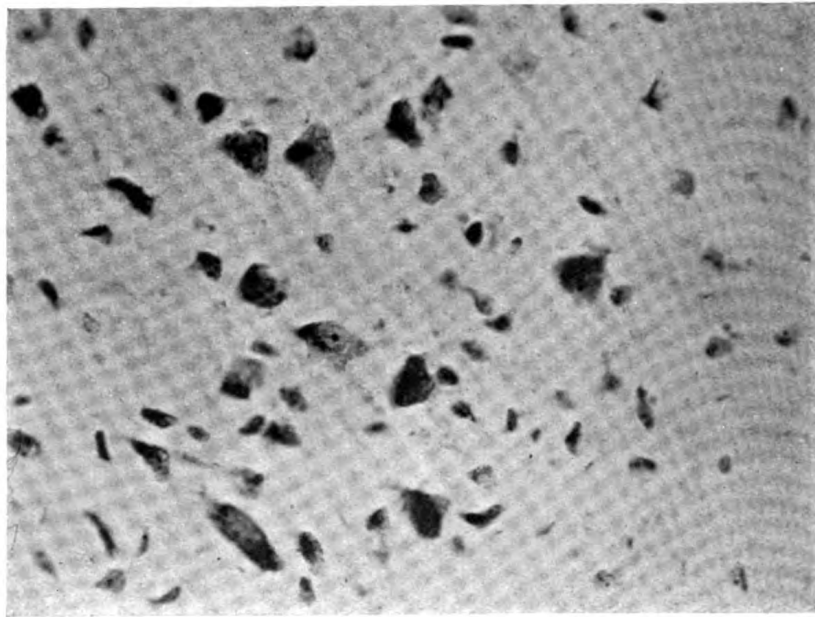


FIG. 19. Cat E. Section of cortex. $\times 400$.

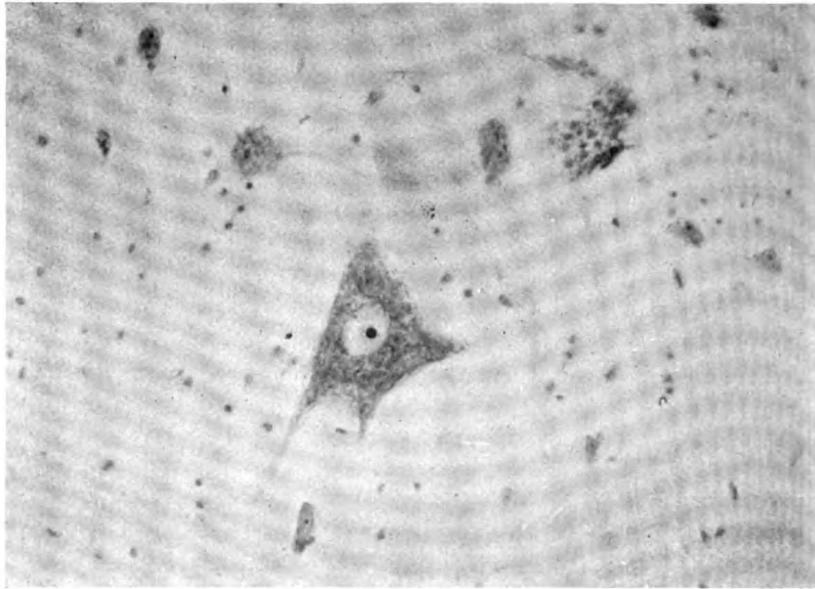


FIG. 20. Rabbit, No. 2. Exposed for 16 hours at 15 cm. 1/4/20; killed 7/4/20. Section of pons. $\times 400$.

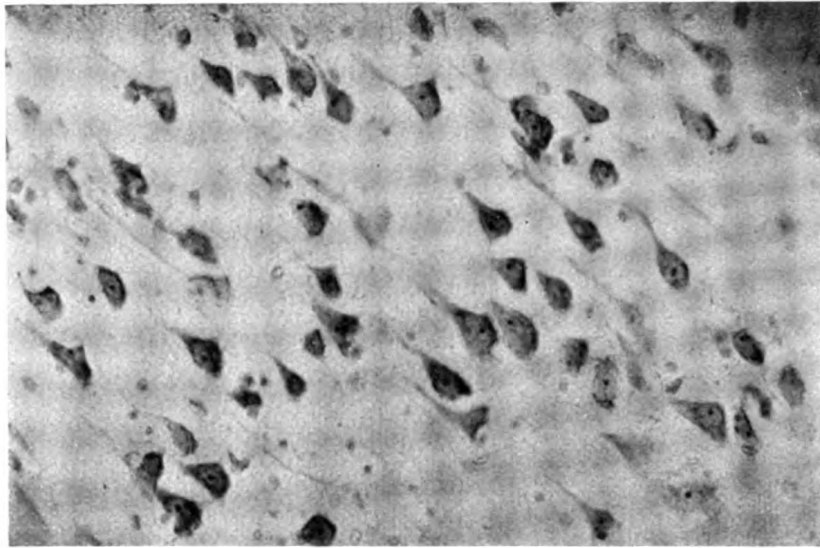


FIG. 21. Rabbit, No. 2. Section of cortex. $\times 400$.

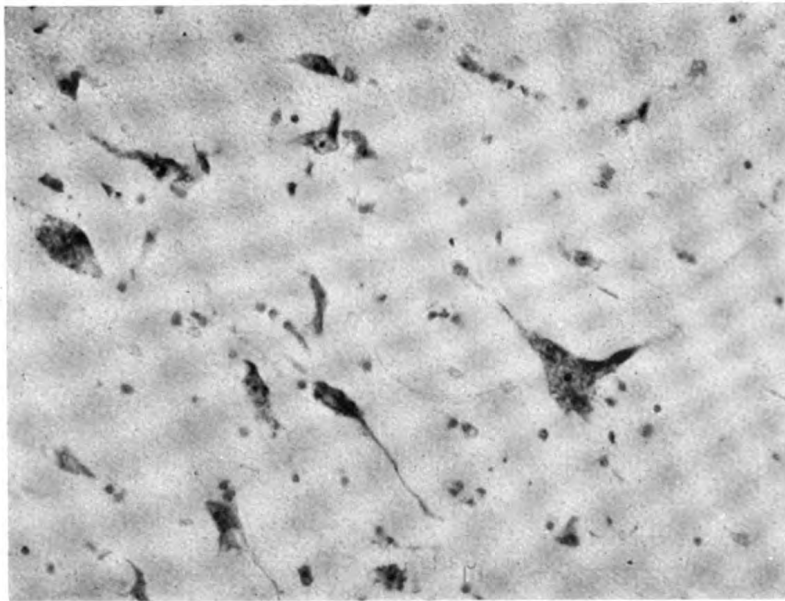


FIG. 22. Rabbit, No. 4. Exposed for 16 hours at 15 cm.; killed immediately after. Section of pons. $\times 400$.

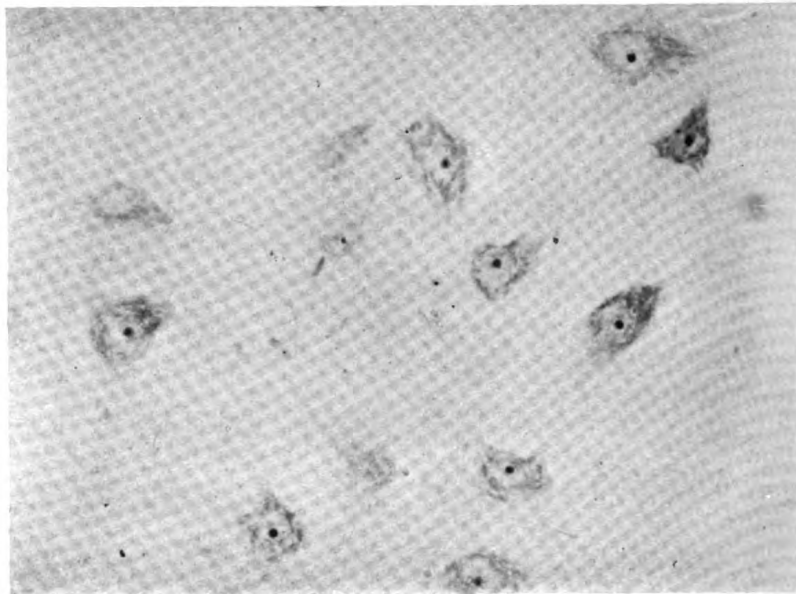


FIG. 23. Rabbit, No. 10. Exposed for 16 hours on each day for 3 consecutive days. Killed immediately after last exposure. Section of pons. $\times 400$.

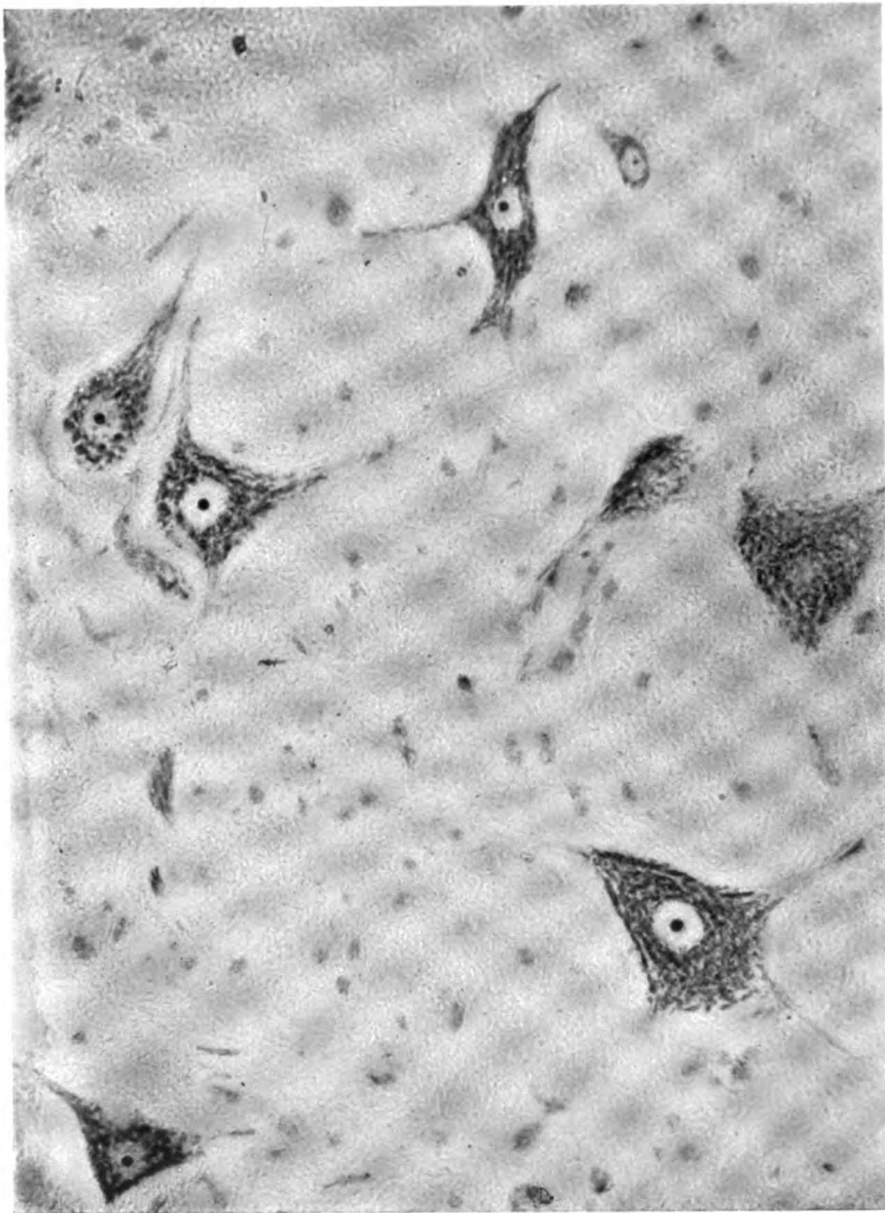


FIG. 24. Rabbit, No. 11. Exposed for 16 hours on each day for 8 consecutive days.
Killed immediately after last exposure. Section of pons. $\times 500$.

- FIG. 25. Purkinje cells of cerebellum. Rat 3.
FIG. 26. Cells of pons. Rat 13.
FIG. 27. Cells of pons. Rat 3.
FIG. 28. Cells of pons. Rat 5.
FIG. 29. Cells of pons. Rabbit 11.
FIG. 30. Two cells of pons. Cat E.
FIG. 31. Cell of pons. Cat A.
FIG. 32. Two cells of pons. Rabbit 4.
FIG. 33. Cell of pons of normal Cat.

$\frac{1}{2}$ oil immersion ocular 6.

Fig. 30.

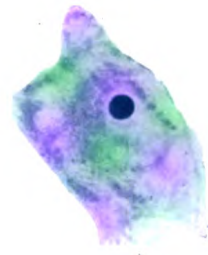
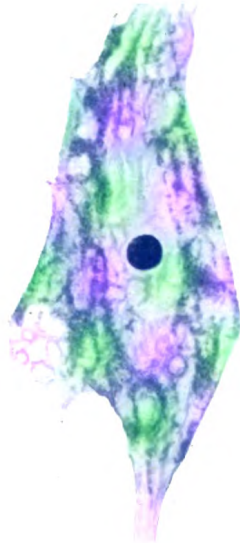


Fig. 31.



J. R. FORD

Fig. 33.

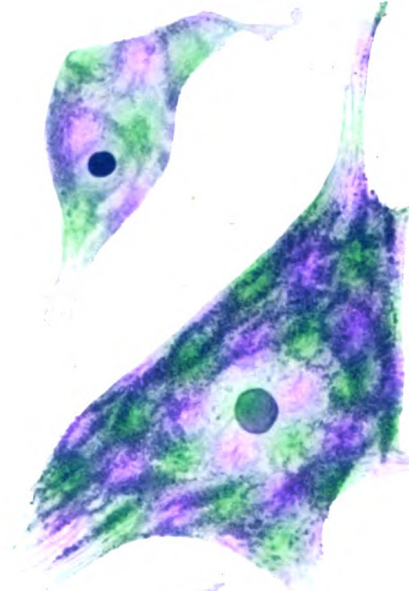
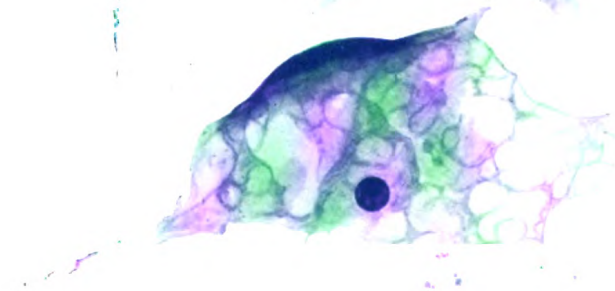


Fig. 32.



[Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY OF MEDICINE,
1921, Vol. XIV (Section of Psychiatry), pp. 23—33.]

The Microscopical Examination of the Choroid Plexus in General Paralysis of the Insane, and other forms of Mental Disease.

By T. MOROWOKA (Kyushu, Japan).

(Communicated by Sir FREDERICK MOTT, F.R.S.)

(ABSTRACT.)

THE following research has been carried out in the Pathological Laboratory of the London County Mental Hospitals, Maudsley Hospital, and I would express my gratitude to the London County Council for permission to work in the laboratory, to the Director, Sir Frederick W. Mott, for his unfailing interest and guidance, and to his staff for their helpful assistance.

MATERIAL.

In all, the choroid plexus from twenty-six cases has been examined ; the mental classification, age at time of death, and pathological conditions found at autopsy are as follows :—

Normal Case.

No 74 : J. McK., male, aged 20. Death from gunshot wound through spinal cord.

General Paralysis of the Insane—Nine Cases.

No. 18 : J. N., female, aged 60. Broncho-pneumonia ; fatty heart ; grave anæmia.

No. 41 : E. D., female, aged 49. Broncho-pneumonia ; bronchitis.

No. 43 : H. M., male, aged 62. Broncho-pneumonia.

No. 45 : C. K., male, aged 42. Broncho-pneumonia.

No. 47 : C. S., male, aged 64. Broncho-pneumonia.

No. 48 : J. W., male, aged 61. Lobar pneumonia ; arterio-sclerosis.

No. 56 : C. J. G., male, aged 43. Early broncho-pneumonia.

No. 57 : C. E. S., male, aged 40. Exhaustion of seizures.

No. 58 : J. W. M., male, aged 62. Gangrene of lungs ; arterio-sclerosis ; renal disease.

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Mania—Seven Cases.

No. 20: L. K., female, aged 60. Senile decay? arterio-sclerosis; broncho-pneumonia.

No. 21: E. M., female, aged 66. Broncho-pneumonia; arterio-sclerosis.

No. 34: H. B., male, aged 37. Pneumonia and gangrene of lungs.

No. 39: S. S., female, aged 39. Broncho-pneumonia; grave anæmia.

No. 40: A. A., female, aged 70. Pneumonia; pneumococcal meningitis.

No. 50: E. K., female, aged 25. Pulmonary tuberculosis.

No. 53: F. T., male, aged 39. Broncho-pneumonia.

Senile Dementia—Two Cases.

No. 33: F. W., female, aged 66. Pneumonia.

No. 44: W. T., male, aged 65. Pneumonia; arterio-sclerosis.

Dementia Præcox—Three Cases.

No. 1: W. H., male, aged 20. Lobar pneumonia.

No. 2: F. R., female, aged 29. Tuberculosis of lungs and intestines; chronic interstitial nephritis; waxy degeneration of liver and spleen.

No. 3: E. G., female, aged 27. Pulmonary tuberculosis.

Epileptic Insanity—Two Cases.

No. 51: M. A., female, aged 32. Congenital weak-minded epileptic; pulmonary tuberculosis; fatty liver.

No. 54: G. H. S., male, aged 37. Epileptic dementia; pleurisy and hypostatic congestion, both lungs; cardiac failure; fatty degeneration of heart.

Alcoholic Dementia—One Case.

No. 42: H. B.: female, aged 53. Arterio-sclerosis; morbus cordis.

Melancholia—One Case.

No. 52: C. B., male, aged 50. Pulmonary tuberculosis.

Arranged in ages at time of death the numbers are as follows:—

70 years and over	1
60-69 "	9
50-59 "	2
40-49 "	4
30-39 "	5
20-29 "	5
					—
					26

MACROSCOPICAL APPEARANCES.

Except in the cases of general paralysis and cases of advanced age there were no marked pathological changes, but the young epileptic and dementia præcox cases showed cystic growth but not denuded epithelium. In general paralysis the choroid was usually enormously fibrosed and appeared like a cord, with almost complete denudation of epithelium. There were no marked pathological changes seen in the cases of mania and melancholia except those which could be accounted for by advancing age, and even the older cases showed comparatively but little fibrous change.

STAINING METHODS.

In the majority of instances the bodies were injected through the carotid arteries with Ringer's or saline solution, the choroid plexuses preserved in 5 per cent. formalin solution, sections cut by freezing microtome method or from paraffin blocks and stained by the following methods:—

- (1) Herxheimer scharlach R.—hæmatoxylin method.
- (2) Lorrain Smith Nile blue method.
- (3) Mann methyl blue—eosin method.
- (4) Ranke Victoria blue method.
- (5) Nissl methylene blue method.
- (6) Nissl toluidin blue—eosin method.
- (7) Unna polychrome methylene blue method.
- (8) Heidenhain hæmatoxylin—eosin method.
- (9) Delafield hæmatoxylin—eosin method.
- (10) Weigert hæmatoxylin resorcin—fuchsin method.
- (11) Unna orcein method for elastic fibres.
- (12) Van Gieson picro-fuchsin—hæmatoxylin method.

The first four methods were found to give the most instructive preparations, and the remainder were used for purposes of confirmation.

The methods of Herxheimer and Lorrain Smith were of great value in demonstrating fatty and lipoid changes. By the latter method the granules of the choroid epithelial cells show central deep blue staining, the membranes of the granules purple blue, with the intermediate zone unstained or of a pale greenish colour. The cell-membranes, the nuclear membranes and myelin sheaths generally stain a purple violet tint. With the selective staining reaction of Nile blue I have been able to demonstrate the presence of lipoid of cholesterol nature and neutral fat, showing as red and purple stained large and small masses in the epithelial cells and especially in the degenerating connective tissue of the choroid plexus in dementia præcox.

In this investigation I have introduced the following modification in Mann's methyl blue—eosin method. The tissues (paraffin sections) are passed through xylol and alcohols, and placed in 0·5 per cent. acetic acid for a quarter to one hour. After thorough washing in tap-water, they are stained for twenty-four to forty-eight hours at room temperature with Mann's original methyl blue eosin solution. The tissues are now tap-water-differentiated, with frequent changes, until a colour cloud no longer appears. They are now developed with 0·5 per cent. acetic acid solution for one hour; the normal tissue appears pale blue whereas the eosinophil substance stains bright red, and the contrast is excellent. After thorough washing with distilled water, they are passed through aniline oil—alcohol mixture, originum oil, benzene, and mounted in benzol-resin. The use of this modification obviates fixation with solutions of heavy metals, and by the use of the aniline-oil mixture, the troublesome and uncertain differentiation with alkali and acid is no longer necessary. The sections are lighter and more transparent; and the pure navy blue and bright red stains afford an excellent contrast in pathological cases.

THE NORMAL CHOROID PLEXUS—CASE 74 (AGED 20).

The granules, cytoplasmic membranes, and nuclei of the epithelial cells are well shown by such basophil stains as Nissl methylene blue, toluidin blue, Unna's polychrome and hæmatoxylin, and are not stained by acidophil stains such as eosin, acid fuchsin, resorcin and orcein.

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By Mann's methyl blue eosin method the epithelial cells, together with the endothelium and connective tissue stroma, are stained pure navy blue without the slightest trace of eosinophil reaction. Victoria blue (Ranke method) stains morbid sclerotic tissue of the choroid plexus a characteristic violet; the nuclear and cellular membranes as well as the granules of the normal plexus cells, together with the endothelium and connective tissue stroma take a very poor and faint violet stain. With the Herxheimer scharlach R. method, the lipid granules of the epithelial cells appear orange coloured and the endothelium and connective tissue stroma show no marked coloration. In this case there was no evidence of hyaline concentric degeneration, cystic metamorphosis or calcareous concretions.

PATHOLOGICAL CHANGES.

The morbid changes observed in the choroid plexus in the twenty-six cases examined may be divided into the following stages :—

(a) Hypersecretion phenomena of epithelial cells, epithelial cell proliferation and formation of pseudo-colloid cysts. The hypersecretion phenomena are evidenced by distension of cells and nuclei, and swollen and distended tubules, especially in the central parts, and the presence of lipid and chromatin granules, with usually some degree of epithelial cell proliferation of smaller cells with larger distorted nuclei. This has been shown experimentally by Pettit and many others.

(b) Acidophil staining of the epithelial cells and fibrous stroma.

(c) Fibrous tissue proliferation and cystic degeneration. Accumulation of cholesterol in the epithelial cells and fibrous stroma. Concentric bodies of a steatotic nature.

(d) Calcareous degeneration.

(e) Extensive epithelial cell destruction, denudation of the choroid plexus, and necrosis of the fibrous stroma.

All these morbid changes are seen to a marked degree in general paralysis of the insane. In this disease and also in the cases of senile dementia examined the choroid plexus showed a remarkable diminution of chromatin substance of both basophil and oxyphil character, also of lipid granules. Moreover, and especially in the later stages of these diseases, the plexus was very poor in villosity, with more or less completely denuded epithelium, and with considerable hypertrophy of the connective tissue and endothelial components: showing various forms of morbid metamorphosis—connective tissue hypertrophy and endothelial degeneration of the villi; amyloid, calcareous and lipid metamorphosis of both larger vessels and villi of the choroid plexus. In addition, in these diseases, there is the presence of lipochrome granules in the epithelial cells. In the earlier stages of general paralysis and the few instances of later stages where the epithelial cells still remained, these epithelial cells showed indications of marked hyperactivity.

In the single case of alcoholic dementia examined there were no marked morbid changes observed except general shrinkage of the choroid tissue and a remarkable diminution, almost exhaustion, of chromatin substance and lipid matter. These changes are of interest in view of the fact that alcohol can pass into the cerebro-spinal fluid, but as only one case has been examined, no definite conclusions respecting characteristic changes in alcoholic cases can be drawn.

The six cases of mania and melancholia examined showed the existence of

well-surviving and actively functioning epithelial cells, in which were observed indications of hypersecretion, eosinophil staining of the nuclei and cytoplasm, and further, some degree of fibrous metamorphosis. These changes occurred in all cases, both young and old, showing that advancing age is not the sole cause of degeneration of the epithelium, vascular endothelium and connective tissue of the choroid plexus.

In the case of the two comparatively young epileptics the villosity of the choroid plexus was well-developed, but some villi showed proliferation of the epithelium and hypertrophy of the endothelium and connective tissue stroma. The epithelium and, even more so, the connective tissue stroma and vascular endothelium showed marked lipid degeneration, hyaline concentric lipid metamorphosis and calcareous degeneration. The occurrence of calcareous deposits in a comparatively young case of epilepsy is of considerable interest. While the hypertrophied endothelial cells showed marked eosinophil reaction the epithelial cells showed scarcely any eosinophil granules.

The three cases of dementia præcox examined did not show such marked changes as those met with in general paralysis and other cases. The epithelium was well preserved. The cells were rather smaller and longer than normal and showed a diminution of basophil chromatin matter with a correspondingly increased acidophil reaction. The epithelial cells showed more granular chromatin substance, especially of cholesterol character, and fat droplets. The connective tissue stroma and endothelium show a moderate proliferative fibrous degeneration around the large vessels and villi of the choroid plexus. They show also hyaline and concentric amyloid bodies.

Even the surfaces of large cystic formations met with in these cases are usually covered with flourishing epithelial cells, while the stroma shows an embryonic mucoid metamorphosis of the connective tissue cells and fibres accompanied with forms of fat degeneration. The cells of the stroma are especially abundant in lipid of cholesterol nature and often neutral fat.

The cerebro-spinal fluid has been regarded as the essential fluid for the central nervous system from both mechanical (Majendie) and chemical points of view (Mott and others); in chemical properties it contains suitable nourishing media—sugar, a trace of protein matter, and inorganic salts.

In the infant the choroid gland possibly serves for myelinization, as its development always precedes cerebral growth, and in foetal life the choroid is very rich in fat and glycogen (Luschka, Kollmann, Goldmann, Pellizzi and Monakow). I have found this also in the choroid of the new-born child. Its material is supplied probably from other endocrine organs. The choroid gland may be regarded as the main producer and regulator of the normal cerebro-spinal fluid. It is the filter of toxic products and probably absorbs and passes into the blood the katabolic waste products of the nervous system (fatty acids, especially unsaturated types mixed with cholesterol, and similar substances which have a great capacity for oxygen). These products are absorbed and presumably by their direct action of stimulation on the choroidal epithelial cells induce the further secretion of fluid to dilute and neutralize abnormal conditions of it. This is supported by the fact that a solution containing extract of choroidal epithelium obtained from Sir Frederick Mott was found by Halliburton and Dixon to induce increased secretion of cerebro-spinal fluid when injected intravenously into animals. Halliburton and Dixon have also shown that the injection of drugs, &c., that increase the general CO₂ tension increases the flow of cerebro-spinal fluid.

In the abnormal conditions I have investigated the first morbid process

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occurring could be demonstrated histologically as indicative of hypersecretion of the epithelial cells followed by eosinophil and fuchsinophil staining reactions indicating a general acidity of the choroid tissue.

In the non-mental case this eosinophil reaction was not observed, and in some of the other cases examined, with respiratory insufficiency resulting in death from pneumonia, &c., it was not present to any great extent. These facts suggest that the acidophil reactions presented by some of the mental cases are not the result of post-mortem change, also that they cannot have been caused altogether by intercurrent disease causing death, and that they are the result of a condition of chronic acidity arising from cerebral physiological disturbance, probably autotoxic in origin.

It is possible that this acidophil condition causes breaking down of complex colloid combinations with deposition in the choroid plexus, and probable occlusion of the tubules and smaller passages, giving rise to cystic formation. Findlay has suggested that cystic degeneration is nothing but oedema arising from obstruction by hypertrophied connective tissue and concentric bodies. This is probable, but I should regard the hyperacidity of the tissue as the important commencing factor.

In epilepsy and dementia præcox the hypersecretion phenomena and eosinophil reactions were not marked, but in dementia præcox there was abundant lipoid deposition and cystic development; but there was cystic degeneration and fibrous hypertrophy, and even calcareous formation, in the cases of epilepsy examined.

With the cases of mania and melancholia investigated the main abnormal features were hypersecretion phenomena and eosinophil reaction.

The cases of general paralysis showed all forms of degenerative processes, especially enormous fibrous hypertrophy, and complete denudation of epithelium, and these changes were observed in all cases whether young or old, and irrespective of the disease causing death. This would account for the excess of protein present.

Further investigations are in progress and will be published with the full report of the above work.

DESCRIPTION OF PLATES.

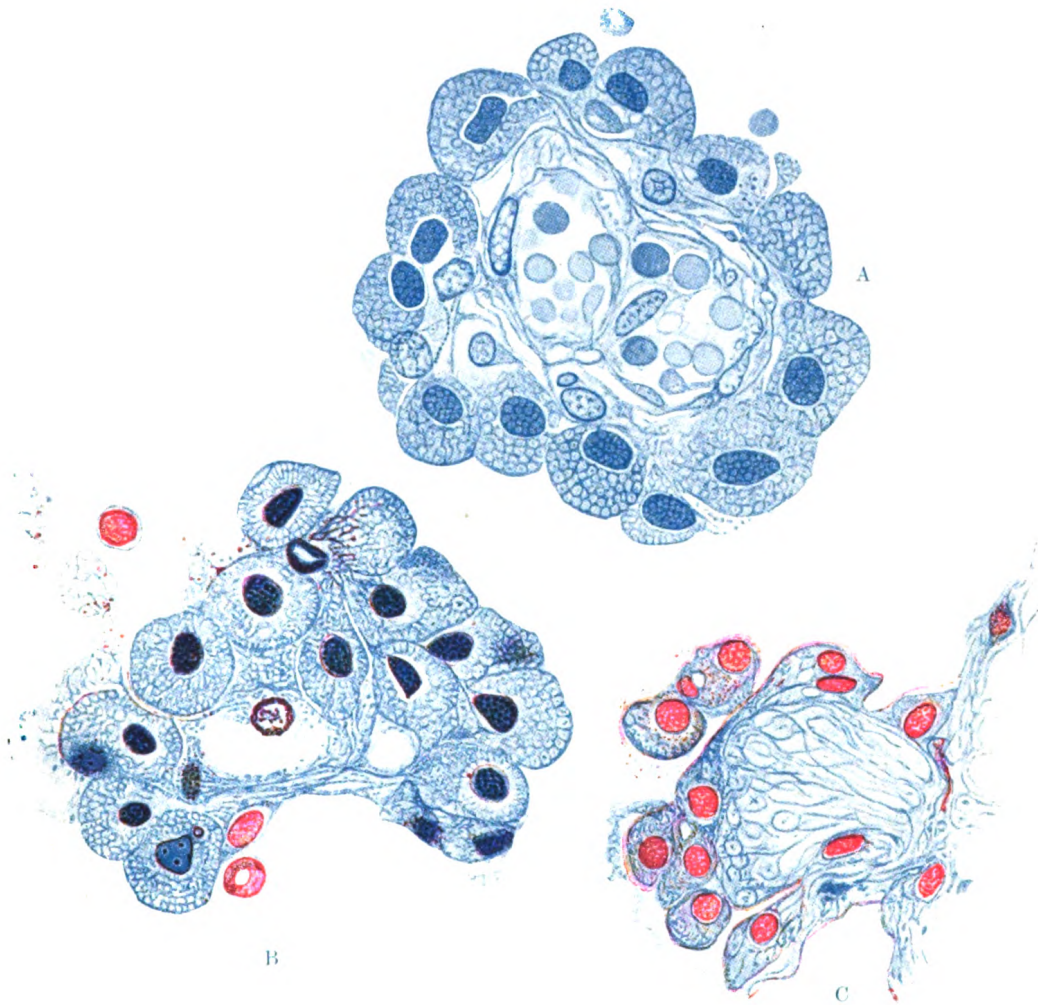
PLATE I.—METHYL BLUE—EOSIN METHOD (MANN).

- A. Normal case. No. 74, aged 20. Showing normal structure of epithelium and absence of eosinophil granules. Endothelium and fibrous structure normal.
- B. Epileptic. Case 54, aged 34. Showing eosinophil staining in endothelium. Epithelium, very few eosinophil granules; the nuclei show homogeneous staining, with cell and nuclear membranes showing slight eosinophil character.
- C. Melancholia. Case 52, aged 50. Showing eosinophil reaction of the epithelial nuclei, with purple-tinted homogeneous cytoplasm, and fibrous hypertrophy.

PLATE II.—METHYL BLUE—EOSIN METHOD (MANN).

Mania. Case 50, aged 25. Showing marked eosinophil reaction of the epithelial cell nuclei, with homogeneous staining and no granularity. A few morula cells (mulberry bodies) are observed, showing distinct granular character. A few amœboid glia cells (Alzheimer) are seen at the bottom of plate lying detached from the epithelium. Fibrous hypertrophy not marked.

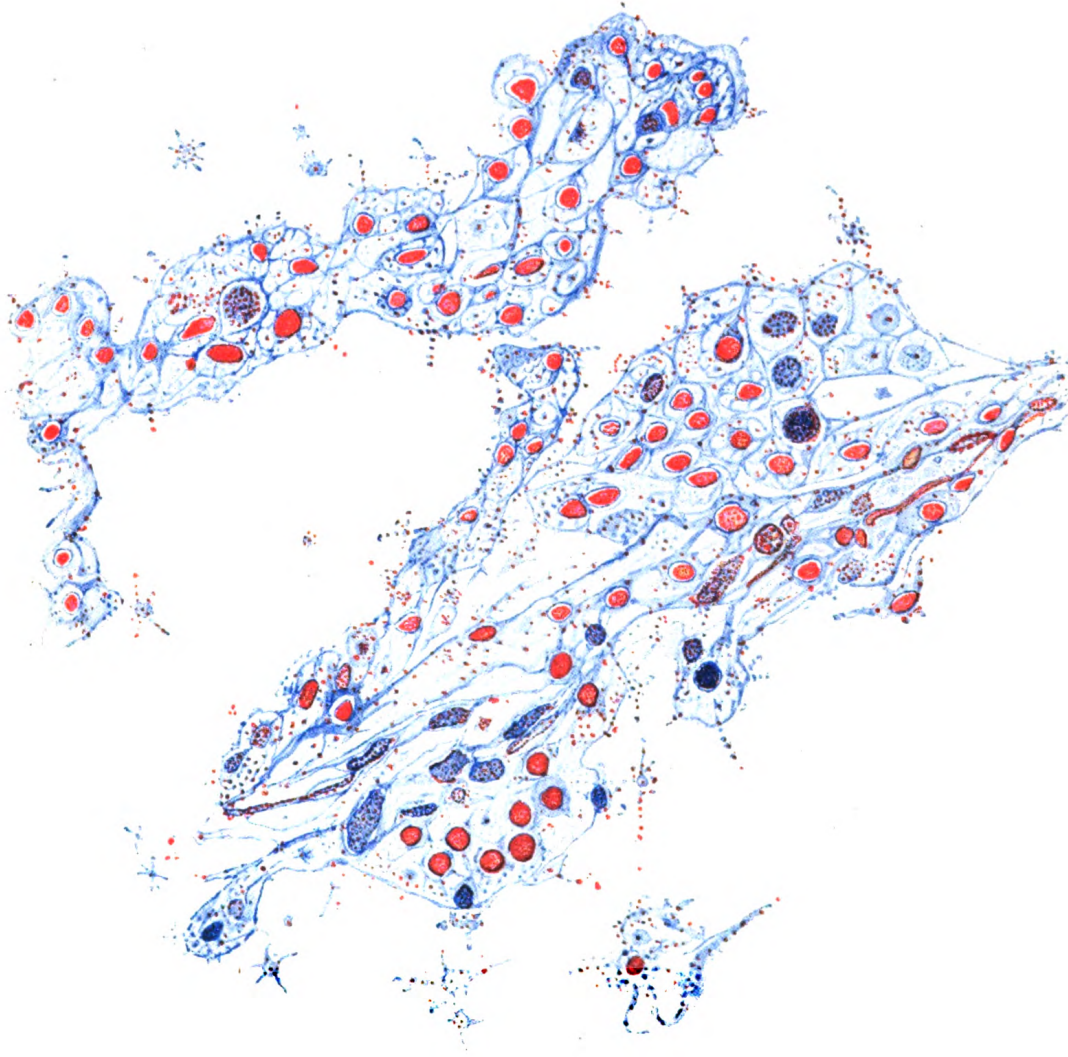
PLATE I.



MOROWOKA :

*The Microscopical Examination of the Choroid Plexus in General Paralysis
of the Insane, and other forms of Mental Disease*

PLATE II.



MOROWOKA :

*The Microscopical Examination of the Choroid Plexus in General Paralysis
of the Insane, and other forms of Mental Disease.*

PLATE III.—METHYL BLUE—EOSIN METHOD (MANN).

- A. Dementia præcox. Case 1, aged 20. Specimen selected from most normal part of tissue, away from areas of cystic growth. Showing moderate eosinophil reaction in the epithelial cell nuclei and cytoplasm. No marked fibrous hypertrophy shown in this specimen, which possibly pictures the earliest stage of degenerative process in dementia præcox.
- B. Alcoholic dementia. Case 42, aged 53. Showing very faint staining, slight eosinophil character and absence of chromatin. Structure, in general, otherwise normal.
- C. Senile dementia. Case 44, aged 65. Showing marked degeneration of epithelium, with slight eosinophil reaction of cytoplasm, and loss of granular structure throughout, especially in the nuclei, and absence of nucleus. Very marked fibrous hypertrophy.

PLATE IV.—METHYL BLUE—EOSIN METHOD (MANN).

General paralysis. Case 47, aged 64. Specimen selected from the most normal part of choroid plexus to show remaining epithelium. Many cell nuclei show eosinophil reaction, with long eosinophil fibres intermingling with each other and ultimately reaching the endothelium. Some cells are shown (*a*) with thread-like processes possibly breaking down fibrous network. Very marked fibrous hypertrophy.

PLATE V.—SCHARLACH R.—HÆMATOXYLIN METHOD (HERXHEIMER).

Dementia præcox. Case 1, aged 20. Selected from normal part of choroid plexus, and stained without acetone treatment. The epithelial cells show large and numerous brown-stained fat droplets and fatty change in the nuclei. Slight hypertrophy of fibrous stroma.

PLATE VI.—SCHARLACH R.—HÆMATOXYLIN METHOD (HERXHEIMER).

General paralysis. Case 47, aged 64.

- A. Low power. Showing very marked fatty deposit in the papillæ and connective tissue.
- B. Medium power. Showing denudation of epithelium, a few degenerated cells only remaining in crevices of the villi. Fatty degeneration in elastic fibres and connective tissue.
- C. Oil-immersion. Showing detailed structure of degenerated epithelium. Fatty changes in endothelium, and epithelial cells and nuclear membranes.

PLATE VII, Figs. 1, 2, 3.—SCHARLACH R.—HÆMATOXYLIN METHOD (HERXHEIMER).

Fig. 1. Normal epithelium of choroid plexus.

Fig. 2. Case 74. Showing slight fatty deposition.

Fig. 3. Case 3 (Dementia præcox). Showing large and numerous lipoid masses. These masses shown so distinctly by scharlach stain; with Nile blue the periphery only takes a purple stain, the central part appearing unstained.

PLATE III.

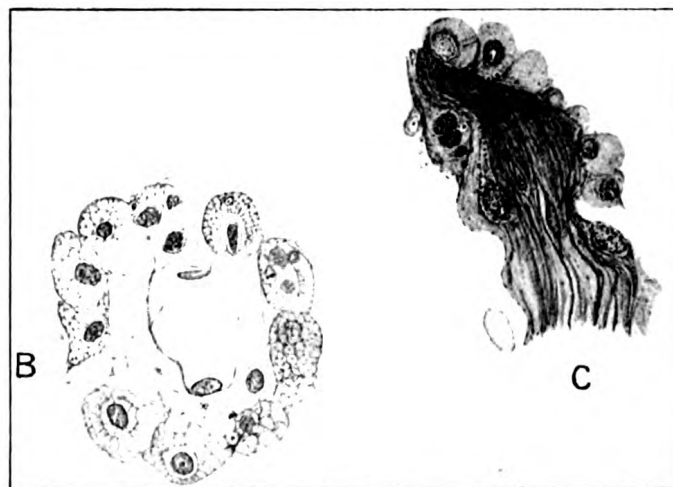
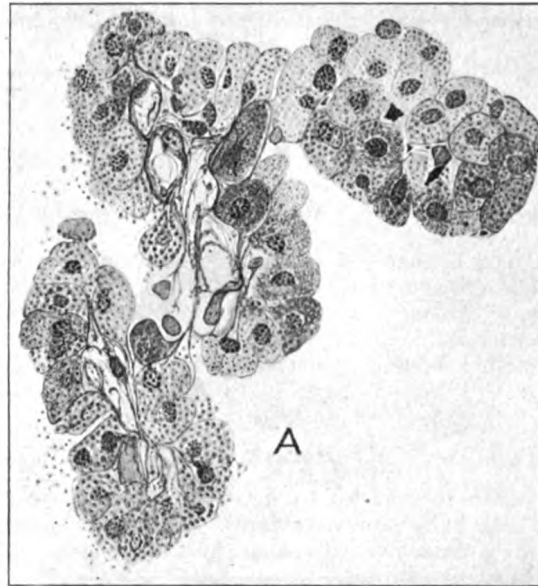


PLATE IV.



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PLATE V.

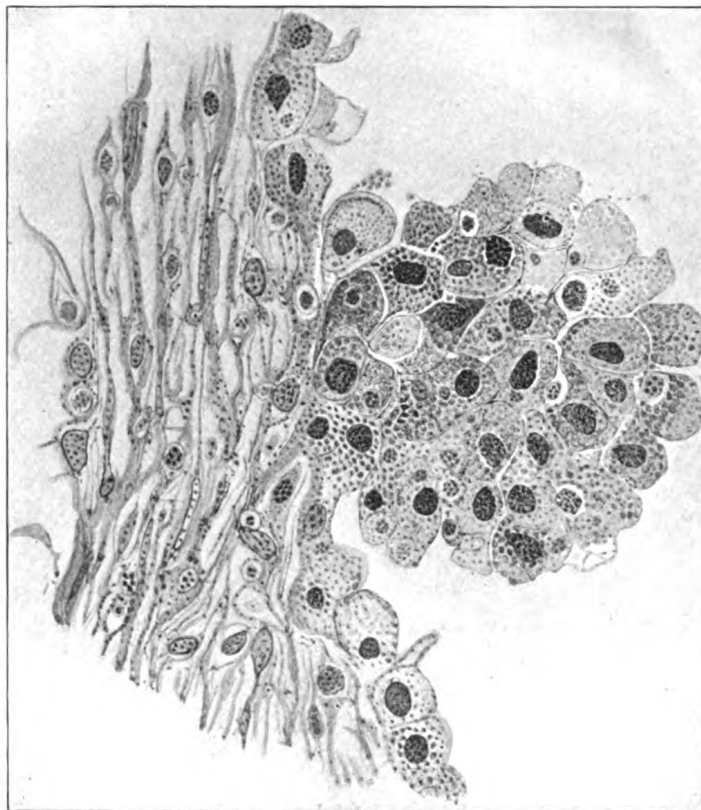


PLATE VI.



PLATE VII.

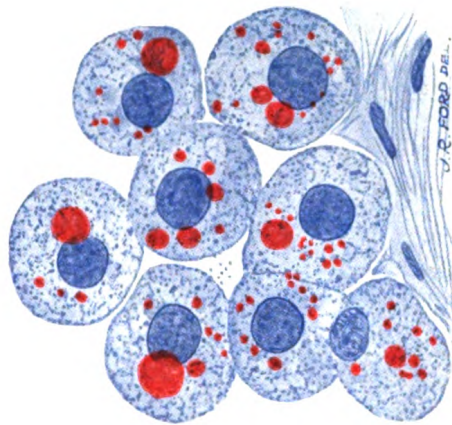


FIG. 3.

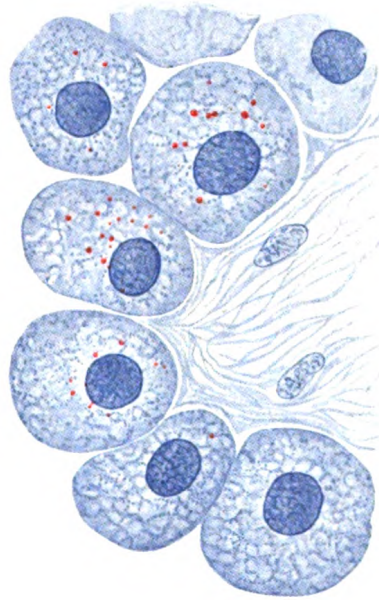


FIG. 2.

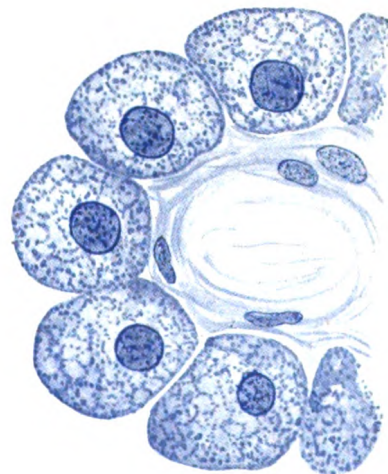


FIG. 1.

MOROWOKA :

The Microscopical Examination of the Choroid Plexus in General Paralysis of the Insane, and other forms of Mental Disease.

Typhoid "Carriers" in Mental Hospitals.

By J. A. GILFILLAN, M.B., Ch.B., D.P.M., and S. A. MANN, B.Sc., A.I.C.

With Note by SIR FREDERICK W. MOTT, K.B.E., M.D., LL.D., F.R.S.,
F.R.C.P.

THE following note is the outcome of an investigation made into the occurrence of typhoid fever at Long Grove Mental Hospital. During the past fifteen months, 13 cases have occurred in six female wards, A, B, C, D, E and F, and Ward B contributed 6 cases, including a fatal case amongst the staff. It is to be noted that the patients from Wards B, C, D and E used the same W.C. during morning and afternoon visits to the hospital gardens; also that all cases were nursed in Ward F. The source of infection of these cases was obscure, and at the suggestion of Sir Frederick W. Mott a detailed bacteriological investigation was carried out in the Pathological Laboratory of the London County Mental Hospitals, Maudsley Hospital, Denmark Hill; the investigation has not only cleared up the source of infection, but also has revealed a condition regarding "carriers" of great importance in institutional hygiene.

In all 90 cases have been investigated. These comprised Group A, all cases who since the opening of the Hospital had given positive agglutination tests, or had been diagnosed clinically as suffering from typhoid fever; and Group B, the immediate contacts.

The blood of these cases was examined, and in all cases giving any degree of agglutination with bacillus typhosus, paratyphosus A or paratyphosus B, the faeces were investigated bacteriologically. The method of examination was the usual isolation of the organism on Maconkey plates, with subsequent identification with sugars and agglutination tests, and in this work we would acknowledge the great assistance rendered by Mr. F. Partner.

GROUP A. In this group—old typhoid cases—the blood of 27 female cases was examined. Of these 13 gave negative agglutination tests, 2 partial, and 12 complete agglutination with bacillus typhosus, para. A or para. B. Examination of the faeces of these positively reacting cases revealed the following carriers:—

1.—CASE E.A. Admitted 11.7.07, previously in Fisherton House and Colney Hatch Mental Hospitals. History negative; no serious illness since admission. During the course of a previous investigation 11 years ago, the blood was found to give a positive Widal reaction (January, 1911), the result of one examination of the faeces at that time was negative, but the specimen was posted to the Laboratory, and it is possible that the organism might have been isolated had the specimen been fresh. At the present time the serum reaction is positive and bacillus typhosus has been isolated from the faeces. This patient, apart from a few days prior to 1911, has been in Ward B since admission, from which ward six cases of enteric fever have been reported.

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2.—CASE H.N. Had enteric fever *over two years ago* (December, 1919); the blood at that time gave a strong positive Widal reaction, and at present there is still complete agglutination in a dilution of 1 in 100. From the faeces the bacillus typhosus has been isolated.

3.—CASE E.B. Had enteric fever *three years ago* (February, 1919). Agglutination tests now completely positive with bacillus paratyphosus A and partial with para. B, and from the faeces bacillus paratyphosus A has been isolated.

4.—CASE R.C. Had enteric fever *ten years ago* (January, 1912); a secondary dement and has been faulty in her habits since 1907; has spent most of her time in Wards A and B. Agglutination tests now positive with bacillus paratyphosus B and partial with para. A, and from the faeces bacillus paratyphosus B has been isolated.

Although no organism has been so far recovered from the faeces, the following case is also worthy of mention:—

5.—CASE I.M. Admitted 8.5.09. Had an attack of enteric fever in September, 1911, with typical clinical manifestations and a positive Widal reaction (B. typhosus). Agglutination now indefinite with bacillus typhosus and strongly positive with bacillus paratyphosus B; examination of faeces so far negative. Since 1911, during mental convalescence and relapse, this patient has been in ten different wards, but has spent most of her time in Ward B.

GROUP B. In this group—contacts—63 female cases were examined, and 7 gave partial agglutination with bacillus typhosus, para. A or para. B, while in one case the agglutination was complete with para. B.

6.—CASE L.T. Readmitted 19.6.14; no history of illness; patient apparently in good health. Has been in five different wards (including Wards B, C, and E) since re-admission. Agglutination test now strongly positive with bacillus paratyphosus B, and this organism has been isolated from the faeces.

Among those cases giving partial agglutination tests in no instance has a typhoid organism been isolated from the faeces.

With regard to Cases 1 and 6, it is worthy of note that one of us (S.A.M.), in the investigation of other slight outbreaks of enteric fever in Mental Hospitals has observed the persistence of positive agglutination tests on the serum of patients with no history of previous illness, and it is very probable that Case I is largely responsible for the occurrence of enteric fever which led to this investigation.

Although it is well known that typhoid bacilli may for long periods remain active in the human subject, the results already obtained from this investigation are rather surprising; five possible "carriers" have been discovered with infective periods varying up to 11 years. Three of these were amongst old typhoid cases, and two in cases with no history of illness; but apart from the discovery of the source of infection the investigation also gives the following important indications.

1. A paratyphoid infection must be considered in all cases of doubtful typhoid fever in Mental Hospitals.

2. The old typhoid case is a source of considerable danger to a Mental Hospital population, and should be controlled by periodic serological and bacteriological examination.

3. The persistence of a positive agglutination serum reaction in a case without clinical symptoms should be regarded with much significance and careful and repeated bacteriological examination of the fæces made before the case is dismissed as a possible carrier. In conclusion we would express our indebtedness to Sir Frederick W. Mott for his unfailing encouragement and interest, and to Dr. Ogilvy, Medical Superintendent, Long Grove Mental Hospital, for permission to utilize the material for publication.

NOTE BY SIR FREDERICK W. MOTT :

I am of opinion that this investigation is of considerable importance in relation to institutional hygiene, and it conclusively shows the danger of spreading infection by the transfer of such cases, and the desirability of notification of a previous infection when a patient who has suffered from typhoid or dysentery is transferred to another ward of the Mental Hospital or to another Hospital.

Seeing the great danger attending the transfer of " carriers " of dysentery, typhoid, and paratyphoid infection, it is very desirable that chronic patients drafted from existing Hospitals should not be used to form the nucleus of the population in a new Mental Hospital without adequate safeguards of their immunity from infectious diseases of this nature. Were this principle adopted we should not see a new Mental Hospital shortly after opening reporting a number of cases of dysentery and typhoid.

(ABSTRACT)

Preliminary Note on the Chemical Examination of the Testes.

By S. A. MANN, B.Sc., A.I.C.

THE following cases have been examined microscopically by Sir Frederick W. Mott, and at his suggestion the chemical investigation has been undertaken.

CASE B. (Maudsley Hospital.) Aged 23. Died 23.1.20. Localized softening of brain (motor aphasia). Inflammation of Lungs.

CASE F. (Maudsley Hospital.) Aged 43. Died 21.2.20. Syphilitic disease of cerebral arteries. Atheroma of Aorta.

CASE A. (King's College Hospital.) Aged 44. Gastric Carcinoma.

CASE G. (Cancer Hospital.) Aged 52. Carcinoma of Tongue.

CASE D. (Cancer Hospital.) Aged 67. Carcinoma of Oesophagus.

CASE E. (King's College Hospital.) Aged 52. Carcinoma of Omentum.

CASE H. (Cancer Hospital.) Aged 64. Carcinoma of Epiglottis.

CASE 2. (Hanwell Mental Hospital.) Aged 21. Dementia Praecox. Lobar pneumonia.

The material was examined by the methods described in detail—Koch and Mann, Archives of Neurology and Psychiatry, Vol. IV., 174, the phosphorus partition being utilized to denote changes in the phosphatide and nucleo-protein constituents.

By this method the following phosphorus fractions have been separated and estimated :—

Lipoid phosphorus. Phosphorus attached to the phosphatide compounds (lecithins, kephalins, sphymgomyelin).

Extractive phosphorus. Water soluble inorganic and organic phosphorus compounds.

Protein phosphorus. Phosphorus in combination with proteins :—nucleo-protein.

TABLE SHOWING PERCENTAGE DISTRIBUTION OF PHOSPHORUS.

Case.	Age.	Weight of Testes.		Percentage of Phosphorus.				Remarks.
		Grammes. R.	L.	Lipoid.	Extractive.	Protein.	Total.	
B.	23	14.7	15.3	0.0490	0.1370	0.0367	0.222	Cerebral Softening.
F.	43	10.5	9.3	0.0515	0.1187	0.0418	0.212	Syphilitic Arteritis.
A.	44	14.0	12.0	0.0598	0.0803	0.0307	0.171	Gastric Carcinoma.
C.	52	10.2	10.6	0.0362	0.0580	0.0247	0.119	Carcinoma of Tongue.
E.	52	14.3	17.6	0.0410	—	0.0210	—	Carcinoma of Omentum.
H.	64	14.7	16.1	0.0285	0.0714	0.0190	0.119	Carcinoma of Epiglottis.
D.	67	10.0	12.0	0.0344	0.0824	0.0271	0.144	Carcinoma of Oesophagus.
2.	21	13.8	15.8	0.0461	0.0954	0.0175	0.159	Dementia Praecox.

The above results are too few to allow any definite correlation of changes found with age, nature of disease, and mental condition, but there is an indication of a diminished phosphorus content in the cancer cases, affecting mostly the extractive and nucleo-protein fractions. The low nucleo-protein figures in the one case of dementia praecox examined is also of interest. (*Vide* Case I, *Studies in the Pathology of Dementia Praecox*, p. 21.)

The work is still in progress, and the results obtained from a larger number of cases will be published later.

(ABSTRACT)

Chemical Investigation of the Blood and Cerebrospinal Fluid in Epilepsy.

By S. A. MANN, B.Sc., A.I.C.

(From the Pathological Laboratory, Maudsley Hospital. Progress Report to the Medical Research Council.)

THE blood has been examined with special reference to possible changes in the sodium, potassium, calcium, and chlorine content, and the cerebrospinal fluid regarding calcium only. The calcium analyses incorporated in this report were made by Dr. Golla.

CALCIUM.

Cerebrospinal Fluid. Calcium determinations have been made on 18 specimens of cerebrospinal fluid from 12 cases of epilepsy and 6 non-epileptic cases. All specimens gave a figure from 8 to 9 milligrammes per cent. calcium, and the epileptics showed no abnormal variations.

Blood Serum. Calcium determinations have been made on 12 specimens of blood serum from 7 epileptics and 5 other cases. The epileptic cases showed an average of 9.7 milligrammes per cent. Ca. with variations from 8.9 to 10.2 mgs. per cent., and the non-epileptics the same average figures with the same variations.

Sodium and Potassium. Determinations have been made on 14 specimens of blood serum from 9 epileptics and 5 other cases. The epileptics showed an average of 0.308 per cent. Na. with variations from 0.292 to 0.339 per cent. The non-epileptic cases gave an average of 0.317 per cent. Na. with variations from 0.304 to 0.330 per cent. The epileptics varied from 14.5 to 27.15 milligrammes per cent. K, and the other cases from 9.9 to 25.1 mgs. per cent. The epileptics showed no consistent departure from the normal, and the apparent variations with all the cases probably finds explanation in slight traces of haemolysis.

CHLORIDES.

Blood Serum. Blood was taken from epileptics before, during and after fits, and 8 cases showed variations from 0.391 to 0.417 per cent. chlorine, four other cases varied from 0.384 to 0.406 per cent. chlorine. In addition the whole blood was investigated in 13 cases, and the following figures show the results obtained and the condition of the patient regarding fits :—

- 1.—0.285% Chlorine Non-epileptic.
- 2.—0.285% „ Non-epileptic.
- 3.—0.285% „ No fits for ten days.
- 4.—0.320% „ Fits daily.

5.—0.285%	Chlorine	Fits two days previously.
6.—0.305%	„	Fits (3) daily.
7.—0.285%	„	Four fits during previous four days, last one morning of test.
8.—0.295%	„	One attack per week, last one night preceding test.
9.—0.280%	„	One attack per two weeks, last one day preceding test.
10.—0.275%	„	One fit per week, last one eight days preceding test.
11.—0.284%	„	Fit night preceding test.
12.—0.284%	„	Fit night preceding test.
13.—0.284%	„	Fit morning of test.

SUMMARY.

The results obtained for the Na, K, and Ca content of the blood, and the Ca content of the cerebrospinal fluid, in epilepsy, come within normal variations, and even in cases in which the blood was withdrawn during a fit no marked changes were observed. The calcium content is of especial interest in view of the work of Loeb, MacCallum, and others indicating that this element may play a considerable part in the chemical equilibrium of the central nervous system, and that an insufficiency may give rise to hyperexcitability, but the results obtained in this investigation do not confirm the work of Parhon (1), who by gravimetric methods indicates a diminution of calcium in the blood in epilepsy, and an increase in melancholia. The figures obtained for the chlorine content of both serum and whole blood do not indicate that there is any marked increase in epilepsy, and that if at the time of fits there is an accumulation of chlorides in the blood, such increase is very temporary, and the normal content is rapidly attained.

(1) Parhon, *Comptes Rendus des Seances de la Société de Biologie*, 82, 1182, 1919.

(ABSTRACT)

Metabolism in Epilepsy compared with the Non-Epileptic as shown by Urinary Excretion.

By E. G. B. CALVERT, M.D., and S. A. MANN, B.Sc., A.I.C.

(From the Pathological Laboratory, Maudsley Hospital, and Maida Vale Hospital for Epilepsy. Progress Report to the Medical Research Council.)

THE comparative metabolism of the epileptic and normal case has been investigated with especial reference to the following urinary partitions:—

- 1.—Nitrogen Partition : Total nitrogen, urea, and uric acid excretion.
- 2.—Phosphorus ,, Total phosphate, alkaline, and earthy phosphate excretion.
- 3.—Sulphur ,, Inorganic, ethereal, and neutral sulphur excretion.
- 4.—Chloride Excretion.

The comparison was made on an adult epileptic and adult normal man, and a boy epileptic and normal boy. Both pairs had exactly the same dietary, the same exercise and confinement to bed, and 24 hour specimens of urine were collected over the same periods.

ADULTS.

- A. Aged 30. Major Epilepsy. For past 4 years has had attacks of major epilepsy once weekly. Weight 11st. 9lbs. Well nourished and developed; not anæmic. No apparent focus of toxic infections and nothing abnormal discovered in various systems.
- B. Aged 43. Normal Man; weight 11 stone.

BOYS.

- C. Aged 13. Epilepsy. *Petit mal* attacks about 20 to 25 per 24 hours, also about two major attacks fortnightly on the same day, sometimes more. Attacks since three years of age. No septic focus of infection, and nothing abnormal discovered in various systems. Weight 5st. 8lbs.
- D. Aged 12. Normal Boy; weight 4st. 8lbs.

The adult epileptic had one major attack at the commencement of the six-day period over which the investigation was made; and the boy epileptic had major attacks during the whole seven-day period.

The total excretions for the whole periods were as follows:—

<i>Adult Epileptic</i> ...	Total Volume of Urine 6,665 c.c.
6 days.	Total Sodium Chloride 57·76 grammes.
<i>Adult Normal</i> ...	Total Volume of Urine 6,354 c.c.
6 days.	Total Sodium Chloride 42·88 grammes.
<i>Boy Epileptic</i> ...	Total Volume 5,832 c.c.
7 days.	Total Sodium Chloride 48·14 grammes.
<i>Normal Boy</i> ...	Total Volume 7,312 c.c.
7 days.	Total Sodium Chloride 57·52 grammes.

Adult Epileptic.

6 days.

Total Nitrogen	...	66.21	grammes.		
„ Uric Acid	...	2.745	„	1.38%	Uric Acid N of total N.
„ Urea	...	112.07	„	79%	Urea N of total N.

Adult Normal.

6 days.

Total Nitrogen	...	56.4	grammes.		
„ Uric Acid	...	1.397	„	0.82%	Uric Acid N of total N.
„ Urea	...	96.59	„	79.8%	Urea N of total N.

Boy Epileptic.

7 days.

Total Nitrogen	...	48.08	grammes.		
„ Uric Acid	...	1.794	„	1.24%	Uric Acid N of total N.
„ Urea	...	87.14	„	84.03%	Urea N of total N.

Boy Normal.

6 days.

Total Nitrogen	...	54.44	grammes.		
„ Uric Acid	...	1.787	„	1.09%	Uric Acid N of total N.
„ Urea	...	103.81	„	88.98%	Urea N of total N.

Adult Epileptic.

6 days.

Total Phosphate as P ₂ O ₅	...	11.06	grammes.		
Earthy „ „	...	3.33	„	30.1%	Earthy P ₂ O ₅ .

Adult Normal.

6 days.

Total Phosphate as P ₂ O ₅	...	10.31	grammes.		
Earthy „ „	...	4.03	„	39.8%	„ „

Boy Epileptic.

7 days.

Total Phosphate as P ₂ O ₅	...	9.5	grammes.		
Earthy „ „	...	2.15	„	22.6%	„ „

Boy Normal.

7 days.

Total Phosphate as P ₂ O ₅	...	10.96	grammes.		
Earthy „ „	...	3.80	„	34.6%	Earthy P ₂ O ₅ .

Adult Epileptic.

6 days.

Total Sulphate as SO ₃	11.58	grammes.		
„ Neutral S. „	...	2.00	„	17.2%	Neutral S.

Adult Normal.

6 days.

Total Sulphate	„	...	11.05	„	
„ Neutral S. „	„	...	1.5	„	9.5% „

Boy Epileptic.

7 days.

Total Sulphate	„	...	9.19	„	
„ Neutral S. „	„	...	0.81	„	8.8% „

Boy Normal.

7 days.

Total Sulphate	„	...	12.07	„	
„ Neutral S. „	„	...	1.36	„	11.2% „

The results show that with both epileptics there is a comparative diminution in the excretion of earthy phosphate ; this has also been noted by Italian observers†. The total phosphate excretion does not show marked variation from the normal, and there does not appear to be any relation between this diminished earthy phosphate excretion and fit periods. In both cases, also, the urinary nitrogen partition shows a comparative increase in the purine nitrogen. These changes were constant day by day and irrespective of the occurrence of fits. The report is of a preliminary nature, and further data are necessary before conclusions can be drawn, but when cases become available with the opening of the Maudsley Hospital, detailed investigations will be made regarding the endogenous purine, and phosphate metabolism in epilepsy and other mental disorders.

† Guidi and Guerri. *Annali dell Istituto Psichiatrico della R Università di Roma.* 67.



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